

## Osteorydin™

### Product Information



**Osteorydin™ Cartilage Support Extract Formulation** is an effective alternative to promote cartilage joint regeneration and TE. It has naturally occurring phytochemical compounds including **Curcuma longa, Polygonum cusputatum, Zingiber officinale, Epimedium grandifolium, Punica granatum, Paeonia lactiflora, Antheum graveolens, Cinnamomum verum** that have a great anti-inflammatory, anti-oxidant, and anabolic potential for the treatment of inflammatory diseases, including the prevention of age-related OA and cartilage TE. It supports cartilage regeneration and TE, which may not benefit from non-steroidal anti-inflammatory drugs (NSAIDs).

Common clinical treatments with chemical agents and synthetic drugs do not have a cartilage-regenerating effect. The cartilage tissue belongs to the family of bradytrophic connective tissues. Due to its unique macro- and microstructural composition and its highly organized structure, cartilage tissue poses a great challenge for researchers who want to repair and regenerate this highly specific tissue. The unique architecture of articular cartilage consists of chondrocytes that produce and are embedded in a cartilage-specific, highly organized extracellular matrix (ECM).

The cartilage-specific ECM is not only synthesized by the chondrocytes, as they are also in close functional interaction with each other and their production in the chondrocytes is stimulated and directly influenced by highly sensitive microenvironmental conditions that stimulate cartilage homeostasis and repair.

**Curcuma longa** exerted anti-apoptotic, anti-catabolic effects on IL-1 $\beta$ -stimulated PCH. Curcumin has potential as an adjunct nutraceutical chondroprotective agent for treating OA and related osteoarticular disorders. Curcumin exerted anti-apoptotic, anti-catabolic effects on IL-1 -stimulated PCH. Curcumin has potential as an adjunct nutraceutical chondroprotective agent for treating OA and related osteoarticular disorders.

**Polygonum cuspidatum**, is abundant in Resveratrol, stilbenes and anthraquinones.. In human chondrocytes, resveratrol has been shown to promote chondrocyte proliferation, the suppression of IL-1 $\beta$ -induced mitochondrial changes, blocking apoptosis, the upregulation of ROS, and the production of the tumor suppressor protein p53 [121]. In addition, resveratrol in combination with curcumin has shown synergistic effects on the suppression of NF- $\kappa$ B pathway activation and the activation of NF- $\kappa$ B-dependent gene end-products involved in inflammation (COX-2, MMP-9, and MMP-13), on the suppression of apoptosis by its inhibition of mitochondrial membrane depolarization and ATP depletion, and on the inhibition of caspase-3 activation. Resveratrol inhibited the expression of VEGF, MMP-3, MMP-9, and COX-2 in PCH stimulated with IL-1 $\beta$ . Resveratrol exerted a chondroprotective capacity by suppression of IL-1 $\beta$ , ROS, p53-production. and apoptosis by down-regulation of NF- $\kappa$ B.

# Extended|Longevity

***Zingiber officinale*** Production of the pro-inflammatory mediators nitric oxide (NO) and prostaglandin E2 (PGE2 ) were significantly reduced with ginger extract in chondrocytes and cartilage explants. Ginger extract reduced IL-1 $\beta$ -induced oxidative stress, mitochondrial changes and apoptosis in chondrocytes.

***Epimedium grandifolium***, or horny goat weed, is an accelerant of growth factors for cartilage TE by promoting chondrogenesis of bone marrow MSCs but not hypertrophy. Ica a is an effective accelerant for chondrogenesis by up-regulation of the expression of aggrecan (AGC), COL2A1, and SOX9 genes. Ica-loaded biomaterials have the potential for cartilage TE.

***Punica granatum*** pomegranate fruit extract (PFE) inhibited the mRNA and protein expression of IL-6, ROS, and IL-1 $\beta$ -mediated phosphorylation IKK $\beta$ , degradation of I $\kappa$ B $\alpha$ , and activation and nuclear translocation of NF- $\kappa$ B/p65 in human chondrocytes. PFE exerted chondroprotective effects by suppressing the NF- $\kappa$ B pathway. PFE inhibited the IL-1 $\beta$ -induced PG breakdown, MMPs expression on protein and mRNA level, p38-MAPK, phosphorylation of inhibitor of kappa B alpha (I $\kappa$ B $\alpha$ ), and NF- $\kappa$ B binding to DNA in OA cartilage explants.


***Paeonia lactiflora***, contains Penta-galloyl-glucose (PGG) known to induce elastogenesis. PGG bound specifically to arterial elastin and preserved the integrity of elastic lamellae despite the presence of high levels of proteinases derived from inflammatory cells. Their results suggested that stabilization of aortic elastin in aneurysm prone arterial segments by PGG offered great potential toward the development of safe and effective therapies for AAAs. Also, PGG-induced vascular relaxation was closely related to activation of a NO-cGMP pathway.

***Antheum graveolens***, Dill Extract Induces Elastic Fiber Neosynthesis. Dill extract (DE) has been demonstrated to stimulate elastin production in vitro in dermal equivalent models and in skin fibroblasts to increase lysyl oxidase-like-1 (LOXL-1) gene expression, an enzyme contributing to tropoelastin crosslinking and elastin formation.

***Cinnamomum verum***, Cinnamon activates the insulin signaling pathway, anti-oxidative pathway and serotonin signaling for its lifespan prolonging effect.

Review

## Herbal Remedies as Potential in Cartilage Tissue Engineering: An Overview of New Therapeutic Approaches and Strategies

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**Abstract:** It is estimated that by 2023, approximately 20% of the population of Western Europe and North America will suffer from a degenerative joint disease commonly known as osteoarthritis (OA). During the development of OA, pro-inflammatory cytokines are one of the major causes that drive the production of inflammatory mediators and thus of matrix-degrading enzymes. OA is a challenging disease for doctors due to the limitation of the joint cartilage's capacity to repair itself. Though new treatment approaches, in particular with mesenchymal stem cells (MSCs) that integrate the tissue engineering (TE) of cartilage tissue, are promising, they are not only expensive but more often do not lead to the regeneration of joint cartilage. Therefore, there is an increasing need for novel, safe, and more effective alternatives to promote cartilage joint regeneration and TE. Indeed, naturally occurring phytochemical compounds (herbal remedies) have a great anti-inflammatory, anti-oxidant, and anabolic potential, and they have received much attention for the development of new therapeutic strategies for the treatment of inflammatory diseases, including the prevention of age-related OA and cartilage TE. This paper summarizes recent research on herbal remedies and their chondroinductive and chondroprotective effects on cartilage and progenitor cells, and it also emphasizes the possibilities that exist in this research area, especially with regard to the nutritional support of cartilage regeneration and TE, which may not benefit from non-steroidal anti-inflammatory drugs (NSAIDs).

**Keywords:** herbal remedies; cartilage; tissue engineering; osteoarthritis; curcumin; icariin; pomegranate; ginger; avocado/soybean unsaponifiables; resveratrol

### 1. Introduction

Currently, about 200 joint diseases are characterized by the term “osteoarthritis” (OA), also known as degenerative joint disease (DJD). OA is reported as the main cause of pain and disability in the joints of older people [1], and the joints most commonly affected by OA are the hip, knee, hand, and spine [2,3]. In addition, it has been reported that 20 percent of adults in Western Europe and North America will be exposed to OA by 2030 [4], and OA can be expected to be a significant economic

## Intersection of Inflammation and Herbal Medicine in the Treatment of Osteoarthritis

Ali Mobasheri

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**Abstract** Herbal remedies and dietary supplements have become an important area of research and clinical practice in orthopaedics and rheumatology. Understanding the risks and benefits of using herbal medicines in the treatment of arthritis, rheumatic diseases, and musculoskeletal complaints is a key priority of physicians and their patients. This review discusses the latest advances in the use of herbal medicines for treating osteoarthritis (OA) by focusing on the most significant trends and developments. This paper sets the scene by providing a brief introduction to ethnopharmacology, Ayurvedic medicine, and nutrigenomics before discussing the scientific and mechanistic rationale for targeting inflammatory signalling pathways in OA by use of herbal medicines. Special attention is drawn to the conceptual and practical difficulties associated with translating data from in-vitro experiments to in-vivo studies. Issues relating to the low bioavailability of active ingredients in herbal medicines are discussed, as also is the need for large-scale, randomized clinical trials.

**Keywords** Osteoarthritis · Rheumatic diseases · Musculoskeletal complaints · Inflammation · Herbal medicine · Ethnopharmacology · Ayurvedic medicine · Nutrigenomics · Clinical trials · Articular cartilage · Synovium · Mesenchymal stem cell · Phytochemicals · Flavonoids · Catechins · Treatment

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### Introduction

The global incidence of age-related diseases of bone, joint, and muscle is steadily rising, seriously affecting the health of millions of people across the world. According to the United Nations (UN) [1] and the World Health Organization (WHO) [2] musculoskeletal, rheumatic, and arthritic conditions are leading causes of morbidity and disability throughout the world, and result in enormous healthcare expenditure and loss of work [3] (sources: The Arthritis Foundation (AF) and WHO [4–6]). The most common and important form of arthritis is osteoarthritis (OA), also known as osteoarthrosis or degenerative joint disease (DJD). OA is the most common type of degenerative joint disease. It is the major cause of pain and disability affecting the elderly [7]. A 2005 study in the USA estimated that OA is one of the top five causes of disability amongst non-hospitalized adults (source: Centers for Disease Control and Prevention, USA (CDC) [8]). According to estimates from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) more than 20 million Americans currently suffer from OA [9]. In 2006, it was estimated that around 35 to 40 million Europeans had OA. It is expected that by 2030, 20% of adults will have developed OA in Western Europe and North America. Therefore, OA is expected to be a heavy economic burden on healthcare systems and community services in Europe and the rest of the world.

Advancing age is a major risk factor for development of OA. There is radiographic evidence of OA in at least one joint in most of the human population aged 65 or over. Although OA is rare in people under 40, it becomes much more common with age. The end stage treatment for OA is surgery, either to modify or replace the joint. With increasing life expectancy, growth of the elderly population, and an alarming escalation of chronic, inflammatory, and age-related conditions (for example OA), there is increased demand for new treatments and preventative approaches.



## Application of Some Herbal Medicine Used for the Treatment of Osteoarthritis and Chondrogenesis

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### Abstract

Rheumatic diseases such as osteoarthritis (OA), rheumatoid arthritis (RA), and low back pain are very popular. The drugs available to treat these diseases are almost ineffective and have significant side effects. There are several approaches used to replace conventional drugs to treat these diseases. One of these methods is the use of herbal medicines. In this study, the effects of herbal medicines and medicinal plants used in the treatment of these diseases include. Searching for articles published in English from 1985 to 2020 using keywords include scientific and traditional names of plants reviewing Scopus and PubMed databases. There is limited research on the anti-rheumatic effects of these plants and the active ingredients. Therefore, further research is needed to determine the mechanism of action, the interaction of effects, the efficacy and safety of medicinal plants, and the potentially beneficial plant nutrients in treatment of these diseases seems necessary. The aim of this review was to update information on OA and chondrogenesis, also importance of herbal drugs for the management of arthritis.

**Keywords:** Herbal medicines; Articular cartilage; Osteoarthritis; Chondrogenesis

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## Botanical Drug Extracts Combined With Biomaterial Carriers for Osteoarthritis Cartilage Degeneration Treatment: A Review of 10 Years of Research

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Osteoarthritis (OA) is a long-term chronic arthrosis disease which is usually characterized by pain, swelling, joint stiffness, reduced range of motion, and other clinical manifestations and even results in disability in severe cases. The main pathological manifestation of OA is the degeneration of cartilage. However, due to the special physiological structure of the cartilage, once damaged, it is unable to repair itself, which is one of the challenges of treating OA clinically. Abundant studies have reported the application of cartilage tissue engineering in OA cartilage repair. Among them, cell combined with biological carrier implantation has unique advantages. However, cell senescence, death and dedifferentiation are some problems when cultured *in vitro*. Botanical drug remedies for OA have a long history in many countries in Asia. In fact, botanical drug extracts (BDEs) have great potential in anti-inflammatory, antioxidant, antiaging, and other properties, and many studies have confirmed their effects. BDEs combined with cartilage tissue engineering has attracted increasing attention in recent years. In this review, we will explain in detail how cartilage tissue engineering materials and BDEs play a role in cartilage repair, as well as the current research status.

**Keywords:** osteoarthritis, botanical drug, extracts, cartilage, tissue engineering, biomaterial carriers

### 1 INTRODUCTION

Osteoarthritis (OA) is a progressive arthrosis disease (Crivelli et al., 2019), the main pathophysiological features of which include cartilage defects, synovitis, osteophyte formation, and subchondral bone damage (Yeh et al., 2015; Wang et al., 2018). OA patients suffer from joint pain and stiffness, difficulty in movement, and ultimately disability (Wang et al., 2018; Jin, 2020), which significantly affects their quality of life (Rahimi et al., 2021), especially for the elderly (Kann et al., 2016), and places a huge economic burden on their families and society (Wang et al., 2018; Jin, 2020). According to the World Health Organization, more than 10% of people under the age of 60 worldwide suffer from OA (Wang et al., 2018). By 2032, the number of people over the age of 45 suffering from OA will increase from 25 to 29%, and the peak of incidence will be around the age of 75 (Qin et al., 2020).