

Eating Well for Healthy Joints

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Osteoarthritis (OA) is one of the most prevalent and disabling chronic diseases affecting older people. It is a degenerative disease of synovial joints that has a major impact on joint function and quality of life. The only resident population of cartilage tissue is represented by chondrocytes, cells synthesizing ECM components and being responsible for cartilage homeostasis [1]. Thus it is clear that the degeneration of these cells is the main event that we need to counteract. The pathological changes in chondrocytes and cartilage are associated with an excessive production of pro-inflammatory molecules, such as interleukin 1 β (IL-1 β) and tumor necrosis factor α (TNF α), which shift the balance between the synthesis and degradation of matrix components resulting in progressive destruction of the joint tissue. Increasing evidence suggests that oxidative stress may be a key pathogenic factor in age-related disorders, such as osteoarthritis (OA), by inducing cell death, hypertrophic differentiation, ECM degradation and mineralization [2]. Besides, dietary and metabolic factors may affect these processes and overall OA development.

So far, there are no efficient therapies for OA and most treatments primarily focus on reducing symptoms, such as relieving pain and improving joint function, without having OA-modifying effects. For example, analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) generally indicated for OA patients have no proved effect on OA prevention and modification. Moreover, long-term administration of these drugs elicits substantial gastrointestinal, renal, and cardiovascular side effects, but on the other hand, given the chronic nature of OA, life-long treatment is definitely required [3].

Why do we have this necessity? Because fighting life-threatening diseases, the lifespan has been extended but this achievement does not imply a good quality of life. A targeted dietary intake or nutraceutical supplementation could meet this request.

The term "nutraceutical" derives from a combination between "nutrition" and "pharmaceutical" and identifies a food or only a component of this with a scientifically proven beneficial effect for our organism. At present, nutraceuticals include dietary supplements at high concentration of a bioactive compound provided from food [4]. The search for molecules in food capable of interfering with the processes that promote the onset or progression of pathologies is of utmost interest to provide indications of an eating style useful for their prevention and to identify new functional foods. The characterization of potential protective mechanisms exerted by these compounds is a major challenge as it would provide molecular bases for their use, thus increasing the therapeutic efficacy of currently available treatments.

Nowadays the most used dietary supplements in OA treatment and prevention are glucosamine and chondroitin sulfate, two of the molecular building blocks of articular cartilage, though their efficacy has not been sufficiently proved. Many compounds such as sulforaphane (an isothiocyanate found in edible cruciferous vegetables, especially abundant in

broccoli), hydroxytyrosol (a polyphenol derived from olives), polyamines (endogenous and food-derived molecules particularly present in wheat germ, rice bran, black rice, Philippine mango, green pepper and many other foods) and n-3 polyunsaturated fatty acids (mainly fish-derived) have been tested in several cellular models, in order to elucidate the molecular mechanisms by which they influence cell viability and signal transduction [5-14]. The characterization of potential protective effects exerted by these compounds in OA may provide molecular bases for their use, thus increasing the therapeutic efficacy of currently available treatments. Indeed, despite the increasing interest on diet and life style effects in relation to OA onset and progression, few data are available to support specific integrations or dietary guidelines. Often classified upon their proven physiological properties, many nutraceuticals have more than a single mechanism of action. Among biochemical pathways investigated as possible targets of nutraceutical supplementation, increasing evidence indicates the critical importance of autophagy that aims to maintain homeostatic balance through removal, degradation and recycling of damaged organelles or proteins. In fact defective autophagy has recently emerged as a feature of articular cartilage in OA-affected joints in both human and in animal models. This process acts in a complex way on cell survival representing a pro-survival mechanism or alternatively acting as a form of cell death. Several studies have reported beneficial effects of autophagy in preventing chondrocyte death, OA-like changes in gene expression and cartilage degeneration. In addition, many microRNAs (miRs) have been identified as key modulators of autophagy pathways. MiRs belong to an abundant, evolutionary conserved subfamily of short non-coding RNAs (22-25 nt) and are identified as potent post-transcriptional regulators able to finely tune protein output and thus entire cellular processes [15-17]. MiRs are promising therapeutic targets as a single miR is able to regulate multiple genes in dysregulated pathways in a disease. So far few relationships have been revealed between nutraceutical compounds and miR network, in particular in OA models. Indeed the unveiling of bioactive compounds, exerting a beneficial effect through induction of epigenetic changes, may open a new topic of research with a huge and not yet well explored potential.

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