

From magnetic ferrofluids to electromagnetic fields in musculoskeletal disorders investigation and treatment

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Introduction: Osteoarthritis (OA) is one of the most common disorders of the musculoskeletal system and is a consequence of mechanical and biological events that modify tissue homeostasis in articular joints. Controlling chondrocyte function and death, cellular response to anabolic and catabolic stimuli, matrix synthesis or degradation and inflammation are some of the targets of chondroprotective treatment, aimed to retard or stabilize the progression of OA. Biological treatments, viscosupplementation, scaffolds, cell cultures, physical treatments are included in complex protocols related to different stages of the disease.

Magnetic ferrofluids mainly consist of nano sized iron oxide particles which are suspended in carrier liquid. Substantial progress has been made in developing technologies in the field of magnetic microspheres, magnetic nanospheres and ferrofluids. Magnetic iron oxide nanoparticles (MION) with a long blood retention time, biodegradability and low toxicity have emerged as nanomaterials for biological applications. MIO nanoparticles have a large surface area and can be engineered to provide a large number of functional groups for cross-linking to tumor-targeting ligands such as monoclonal antibodies, peptides, or small molecules for diagnostic imaging or delivery of therapeutic agents.

Techniques based on magnetisable solid-phase supports (MSPS) have found application in numerous biological fields as diagnostics, drug targeting, molecular biology, cell isolation and purification, radio immuno assay, hyperthermia causing agents for cancer therapy, nucleic acid purification etc. Although often referred to as magnetic, many of the particles currently used are superparamagnetic, meaning that these particles can be easily magnetized with an external magnetic field and redispersed immediately once the magnet is removed. Currently available formats of particles can be broadly classified into unmodified or naked particles, chemically derivatized particles with general specificity ligands (streptavidin, Protein A etc) and chemically derivatized particles with specific recognition groups as monoclonal and polyclonal antibodies. The association of magnetic nanoparticles with hydrogel type biopolymeric shells confers to composite material biocompatibility and the capacity to retain and deliver bioactive substances. We review current development of such targeted nanoparticles covered with antiinflammatory steroids (dexamethazone) and hyaluronates for intra-articular therapy. The superparamagnetic properties, which result from the encapsulation of superparamagnetic iron oxide nanoparticles (SPIONs), allow for microparticle retention with an external magnetic field, thus possibly reducing their clearance from the joint.

Although many drugs or substances have been recently introduced for the treatment of OA, the majority of them relieve pain and increase function, but do not modify the complex pathological processes that occur in these tissues. Pulsed electromagnetic fields (PEMFs) have a number of well-documented physiological effects on cells and tissues including the upregulation of gene expression of members of the transforming growth factor β super family, the increase in glycosaminoglycan levels, and an anti-inflammatory action. The modern bone growth stimulators that employ pulsed electromagnetic fields (PEMFs) have been available for 20 years, although they are just becoming a standard of care for delayed union fracture. A foundation of in vitro and clinical studies has demonstrated that electric and magnetic energy may favorably affect disorders of dense connective tissue.

Until the middle 50's, both magnetically soft and hard materials were produced mostly by melting, casting and hot manipulation.

Powder techniques were being applied on a pilot plant scale only, but during the last two decades these have become predominant and in the future almost all permanent magnets will be produced by this route. The development of new compositions and processes is

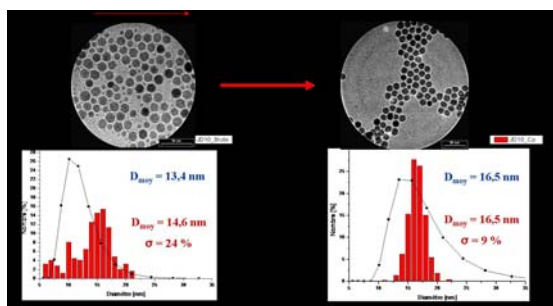


Figure 1 – monolayer magnetic nanoparticles stable in aqueous suspension, for size selection (Institut de Physique et Chimie des Matériaux De Strasbourg)

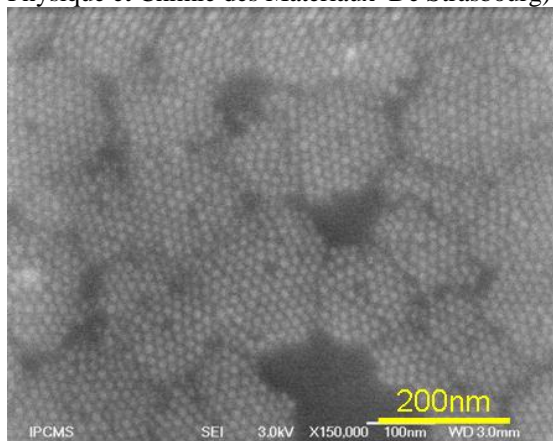


Figure 2 – SEM aspect – 3D multilayer magnetic nanoparticles Langmuir Blodgett technique (Institut de Physique et Chimie des Matériaux De Strasbourg)

traced, with examples of applications, with emphasis on the impact which the latest rare earth cobalt or iron super energy magnets are having in this field.

We also present a magnet-based orthetic device used to control therapeutic superparamagnetic nanoparticles. Its advantages include the ability to permanently keep the nanoparticles coated with therapeutic agents in the targeted area - eg femuro-patellar articulation.

This technique could enable minimally invasive procedures, such as intra-articular injections to be better targeted, and warrants further study in chondral defects with different sizes and locations.

These applications of magnetism have become a fertile area of research in orthopedics and rheumatology.

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