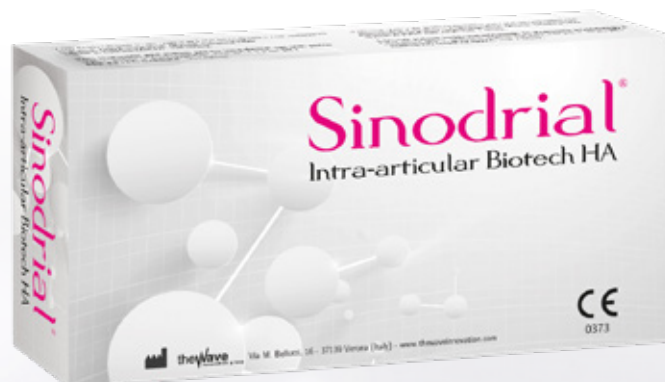


Sinodrial®

INNOVATIVE CONSERVATIVE HA



MULTIFACTORIAL INFILTRATIVE THERAPY
for the maintenance of articular cartilage

INTRODUCTION

Osteoarthritis (OA) is a degenerative disease that affects different tissues of the surrounding joints such as articular cartilage, subchondral bone, synovial membrane, and ligaments. No therapy is currently available to completely prevent the progression of the disease due to poor understanding of the pathology mechanisms.

Articular cartilage is the main tissue afflicted with OA; chondrocytes are cellular components of the tissue that actively participate in the degeneration process.

Multiple factors influence the development and progression of OA including inflammation during disease progression and by the biomechanical alterations of cartilage due to wear and trauma. **During the progression of OA, extracellular matrix (ECM) cartilage is actively remodelled by chondrocytes in inflammatory conditions.**

This alteration of ECM, in turn, changes the biomechanical environment of chondrocytes, which further push the progression of the disease in the presence of inflammation.

Changes in the composition and ECM structure also prevent the participation of mesenchymal stem cells in the cartilage repair process by inhibiting their chondrogenic differentiation.

While all amino acids are susceptible to oxidative alteration, arginine, histidine, lysine, phenylalanine, tyrosine, proline, threonine, tryptophan, glycine, methionine, and cysteine are more subject to increase oxidation of their side chains than other amino acids.

CHARACTERISTICS OF AGED AND DEGENERATED ARTICULAR CARTILAGE

STRUCTURAL

- Stable localized fibrillation.

CELL

- Destruction of chondrocyte density;
- Disintegration of the anabolic response to growth factors;
- Disintegration of synthetic activity;
- Mitotic activity deficiency;
- Synthetic activity altered by aggrecans;
- Diminution of telomere average length;
- Increased replicative senescence.

MATRIX

- Diminution of chondroitin sulphate chain length;
- Diminution of water content;
- Accumulation of degraded aggrecans;
- Smaller variable aggrecans;
- Increased collagen cross-linking;
- Disruption of tensile strength;
- Increased collagen cross linking.



OSTHEARTHRTIS

Knee osteoarthritis (OA) is a common degenerative pathology that occurs as a result of inflammation and abnormal overload of the joint, with the consequent biochemical and morphological changes of the joint.

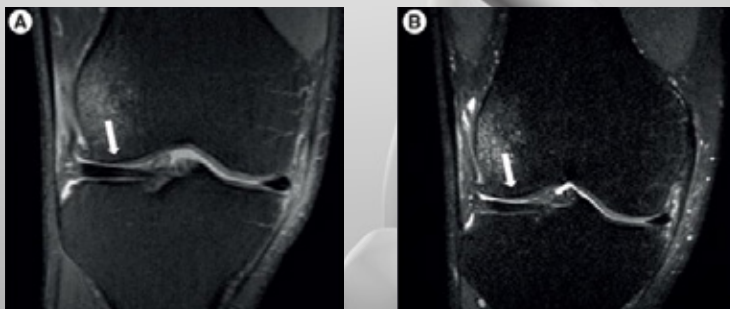


The arrows indicate the cartilage and subchondral bone modification characteristic of osteoarthritis of the patellar femur.

Often in idiopathic knee OA, degenerative changes manifest themselves before morphological changes in the joint.

The cartilage of the knee is the main tissue subject to degeneration.

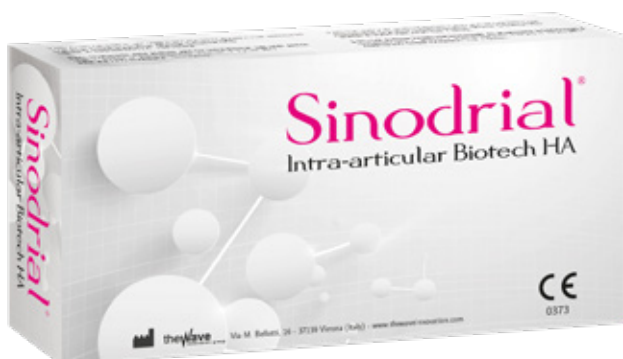
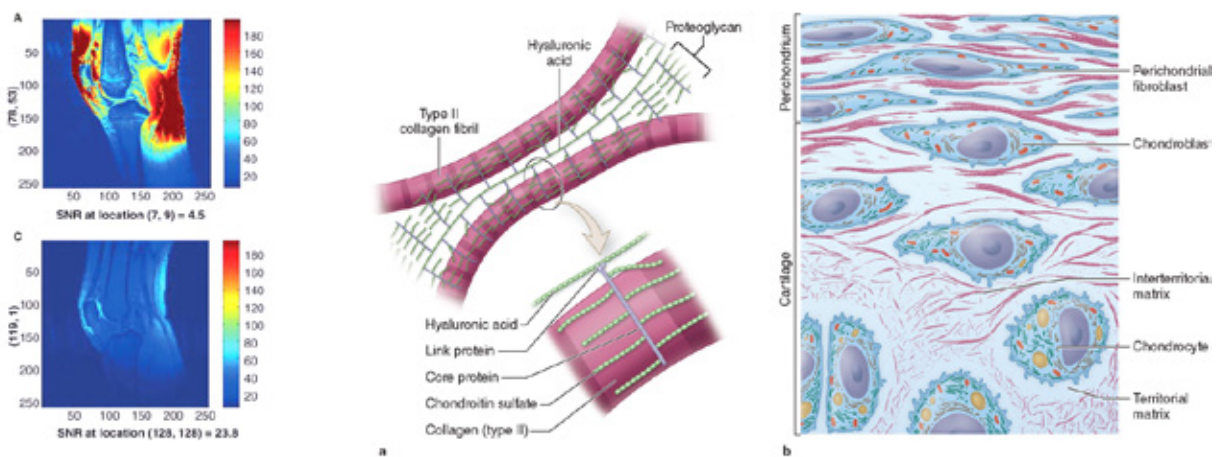
Articular cartilage is a non-vascularized and non-enervated connective tissue whose capacity is to resist stress and compression, is composed of a single cell population, the chondrocytes, which are able to maintain tissue homeostasis.



A small fissure in the cartilage in the medial condyle of the femur is shown with VIPR ATR images in the sagittal (A) and coronal (B) planes.

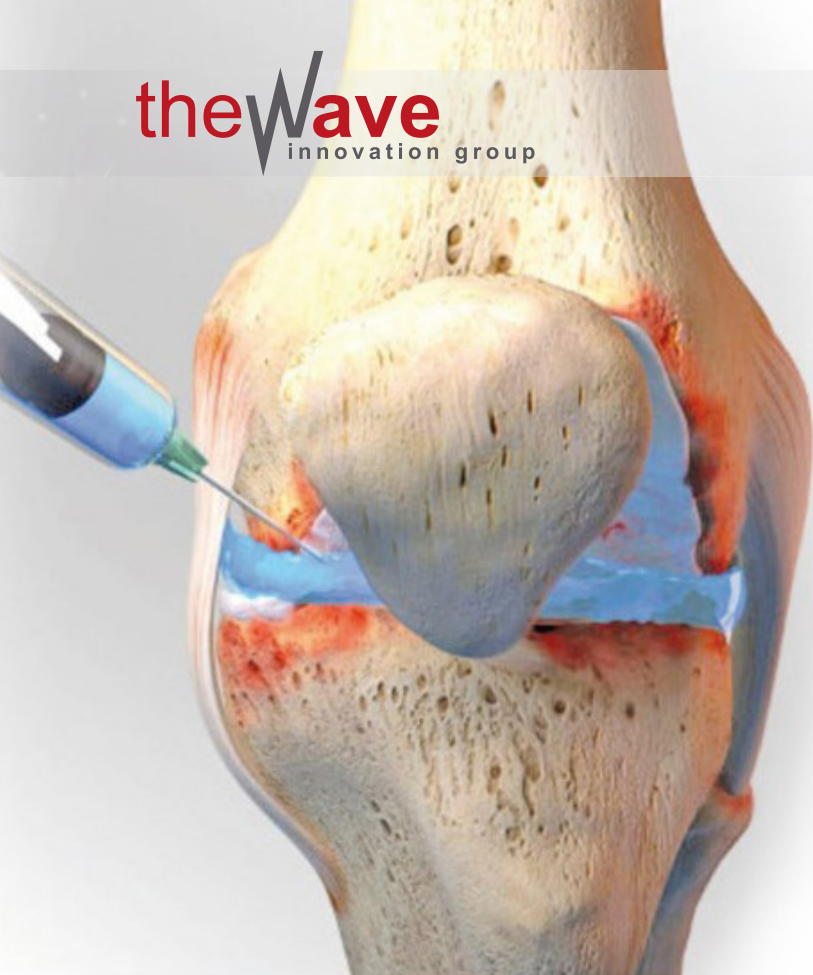
JOINT CARTILAGE

Adult articular cartilage is an avascular tissue composed of a specialized matrix of collagens, proteoglycans and proteins, in which the chondrocytes constitute the only cellular component. Cartilage is a highly effective water-based tribological system that is optimized to provide low friction and wear protection at both low and high loads (pressures) and sliding speed that must last for life.



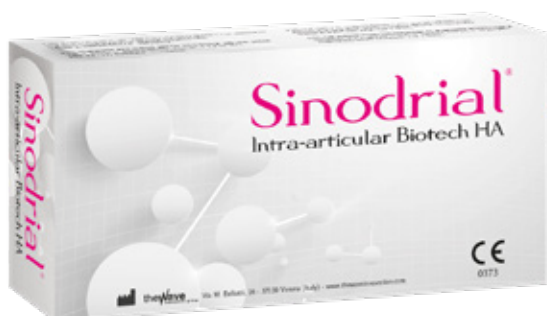
Hyaluronic acid (HA) is abundant in cartilage and synovial liquid and has a main role in the joints.

HA with the glycoprotein lubricant (LUB) form a reticulated network fundamental for the mechanism of prevention of joint wear.



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In the last two years THE WAVE Research & Development has directed some studies concerning the activity of particular amino acids, precursors and hyaluronic acid with specific molecular weights.

We used a set of specific amino acids and precursors with different characteristics and a hyaluronic acid with a high molecular weight that allows the synovium to produce proteins present in the synovial fluid, removes impurities and stimulates the proliferation of chondrocytes.



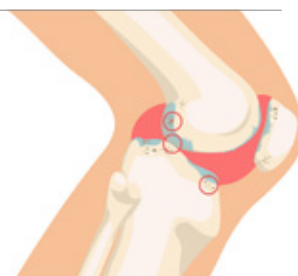
STAGE I
DOUBTFUL



STAGE II
MILD



STAGE III
MODERATE



STAGE IV
SEVERE



2 SYRINGE PER BOX

PROTOCOL / DOSAGE:

- 1 syringe each 15 days for 2 months (4 syringes)
- At 6 months 1 syringe

INNOVATIVE CONSERVATIVE HA

SINODRIAL demonstrates in its clinical activity to activate metabolic and conservative processes of articular cartilage, the hyaluronic acid hydrogel with precursors and amino acids stimulates the chondro-degeneration with cell surface receptors, increases the type II collagen production, and positively influences in the capacity of the chondrocytes to maintain at all the extracellular matrix (ECM), cartilage and joint structure.

SINODRIAL is a synovial fluid substitute which, thanks to its viscoelastic and lubricating properties, promotes the maintenance of the rheological conditions of the degraded articular cartilage in patients with degenerative knee osteoarthritis.

SINODRIAL improves the characteristics of the synovial fluid of the knee, exerting a protective and reparative action on the joint with consequent improvement in functionality and reduction of painful symptoms. SINODRIAL acts only at the level of the joint in which it is injected, without exerting any systemic action.



SINODRIAL IS A SINOVIAL FLUID REPLACER THAT HELPS MAINTAIN THE RHEOLOGICAL CONDITIONS OF ALTERED JOINTS

STAGE 3 OF OA

SINODRIAL is a Sterile injectable medical device class 3 for intra-articular use.

In one box there are 2 pre-filled syringes containing 2ml/50mg (2,5%) of non-pyrogenic gel, sterilized using moist heat.

SINODRIAL is composed for a HA molecular weight of 3 million DA already sterelized, animo acids and precursors: hidroxyproline, proline, glycine and lysine,...

RESULTS:

- ACTIVATES METABOLIC AND CONSERVATIVE PROCESSES OF ARTICULAR CARTILAGE THANKS TO THE HYALURONIC ACID HYDROGEL WITH PRECURSORS AND AMINO ACIDS;
- STIMULATES THE CHONDRO-GENERATION WITH CELL SURFACE RECEPTORS;
- INCREASES THE PRODUCTION OF TYPE II COLLAGEN;
- POSITIVELY INFLUENCES THE ABILITY OF CHONDROCYTES TO MAINTAIN THE EXTRACELLULAR MATRIX, CARTILAGE AND JOINT STRUCTURE;
- IMPROVES THE CHARACTERISTICS OF THE SINOVIAL FLUID OF THE KNEE;
- EXERTS A PROTECTIVE AND CONSERVATIVE ACTION ON THE JOINT;
- IMPROVES IN FUNCTIONALITY AND REDUCTION OF PAINFUL SYMPTOMS.



TRAUMATOLOGY
AESTHETIC MEDICINE
UROLOGY / GYNAECOLOGY
COSMETICS
DERMATOLOGY
NUTRITION
DENTAL

The Wave Innovation Group is an Italian pharmaceutical company founded by Dr. Salvatore Terrani in 2016 with a great experience in the hyaluronic acid injectable medical device sector (class III) and in the pharmaceutical sector.

The Wave Innovation Group was born from the need to produce and market innovative medical devices, created and developed in partnership with **The Wave Research & Development**; this collaboration allows to cooperate with the leading R&D companies and pharmaceutical companies worldwide.

The Wave Innovation Group can manage the entire production process of injectable medical devices (class III) at its production hub, operating under the ISO 13485 regime with particular attention and quality control.

The Wave Innovation Group holds patents on the injectable medical devices that markets and holds those under development.

This has allowed us to build a diversified product portfolio in multiple Therapeutic areas, which include: drugs, medical devices, food supplements and health products.

The Wave Innovation Group is supported by two prestigious Italian Universities: the Luigi Vanvitelli of Naples and the STEBICEF University of Palermo, which are entrusted with all preliminary scientific studies of first, second and third phase.

The Wave Innovation Group has over 50 distributors worldwide in Europe, Asia, Middle East and Latin America.



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