



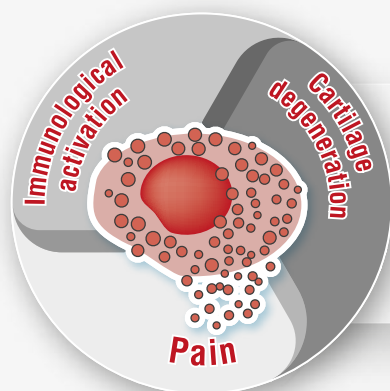
hyadrol[®]

Innovating
Intra-articular Injection Treatment
with Adelmidrol

Overall action on the mechanisms
sustaining the impaired joint metabolism

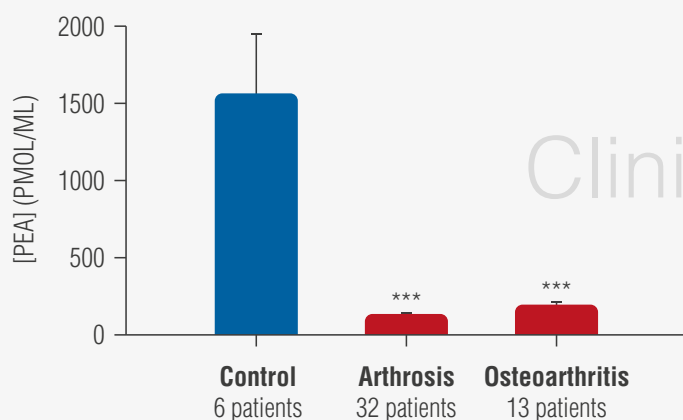
Articular degenerative diseases: a complex issue

The most recent scientific evidence show that **Degenerative Joints Diseases** are characterized by a multifactorial alteration affecting the articular metabolism

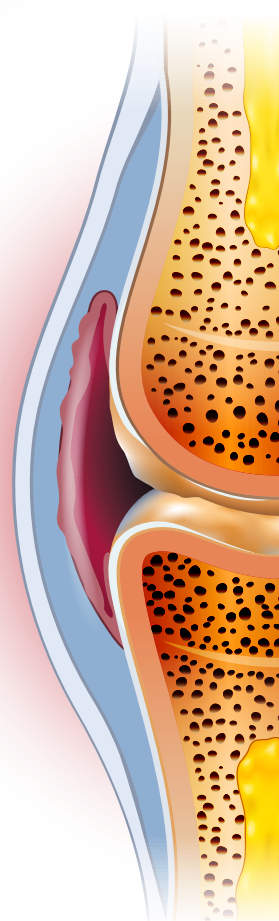


Acting on the mast cell regulation (*innate immune system*) allows an overall management of the joint degeneration

The **dramatic reduction** of **Palmitoylethanolamide (PEA)** levels, an endogenous lipid provided with remarkable mast cell-modulating properties, is a signal of a multifactorial alteration of the joint metabolism in subjects with **Arthrosis** or **Osteoarthritis**

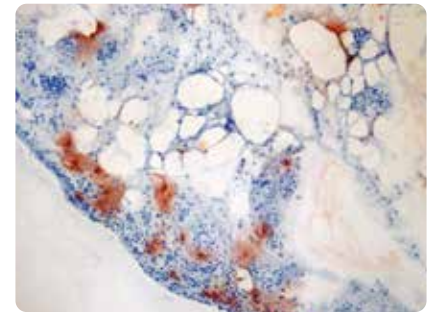


Clinical study



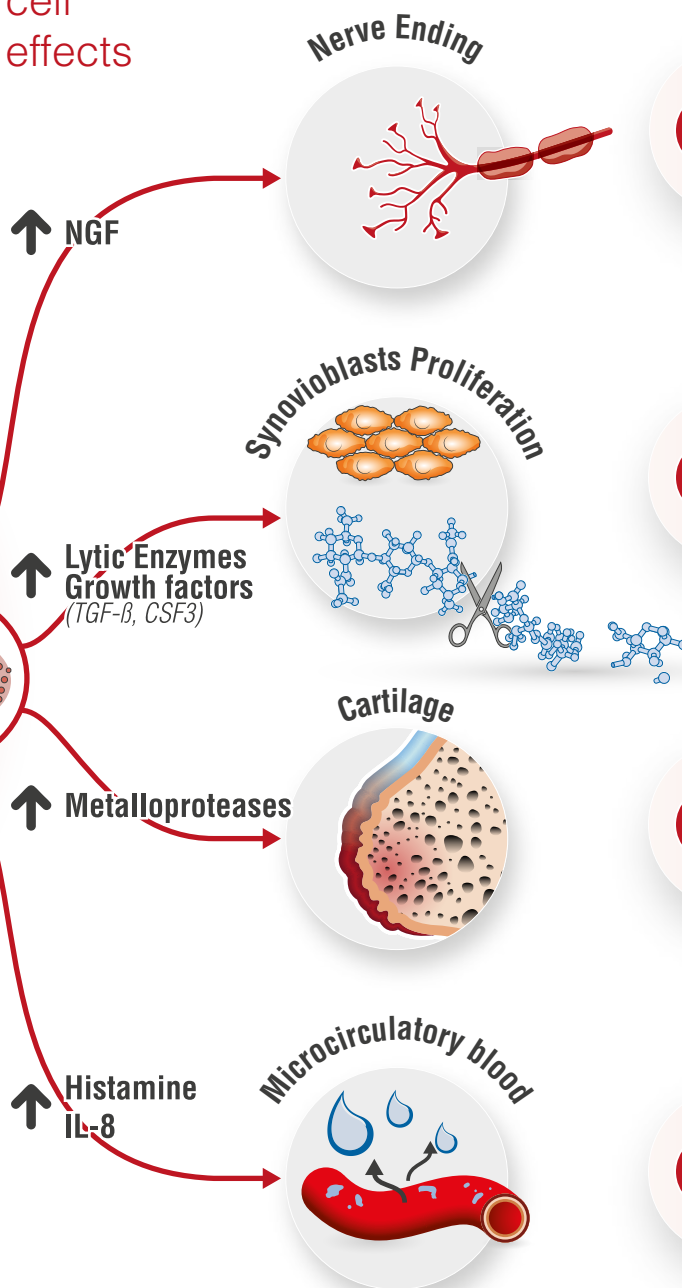
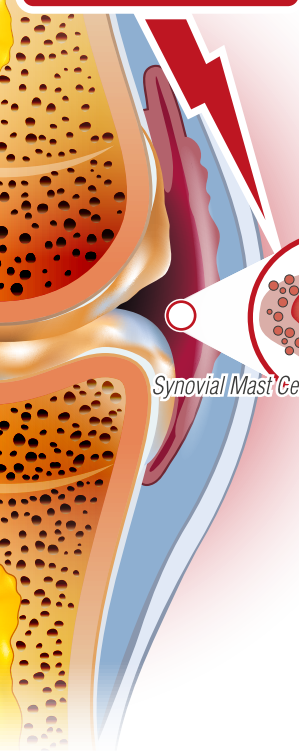
Mast cells and the impaired joint metabolism: how?

Mast cells count increases in the synovial membrane during Joint Degenerative Diseases. ^(1; 3)



Synovial mast cell degranulation effects

Activating stimuli
(i.e. mechanical, immune-inflammatory)



Neuroinflammation and **Joint Pain** ^(7; 8)

Degradation of the native hyaluronic acid **Joint Stiffness** ^(1; 2; 9)

Progressive cartilage erosion and **Osteochondrosis** ⁽¹⁾

Plasma extravasation and **Intrarticular Effusion** ^(1; 2; 10)

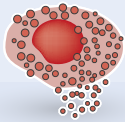
hyadrol[®]

Adelmidrol 2%
Hyaluronic acid 1%
high molecular weight

Adelmidrol 2%

Vehicle: a Hyaluronic acid bio-binding epitope*

PEA
⊥

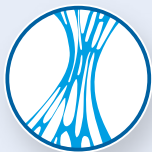


hyadrol[®] increases the levels of **Synovial Palmitoylethanolamide**⁽¹²⁾

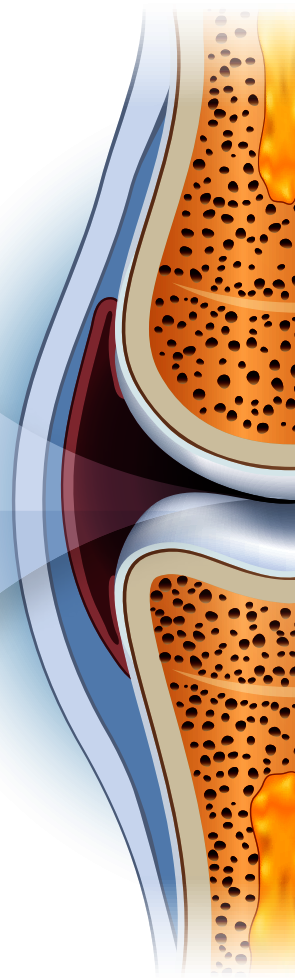
Palmitoylethanolamide, modulating the synovial mast cell (ALIA mechanism), reduces the **release** of **pro-neuroinflammatory mediators**.⁽¹³⁾



hyadrol[®] slows the degradation of the **injected hyaluronic acid**.^(5; 14)

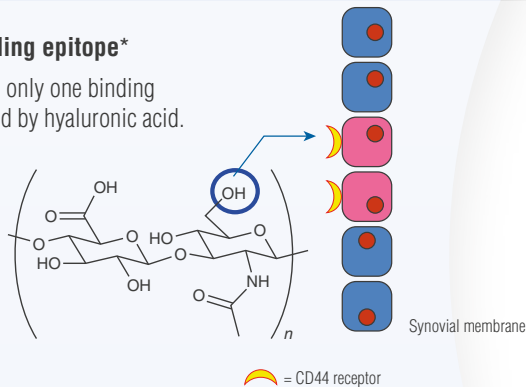


hyadrol[®] allows for **prolonged bioadhesion** and optimizes the natural **visco-induction** process.^(11; 15; 16)



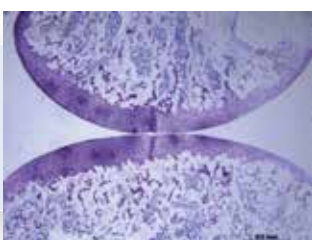
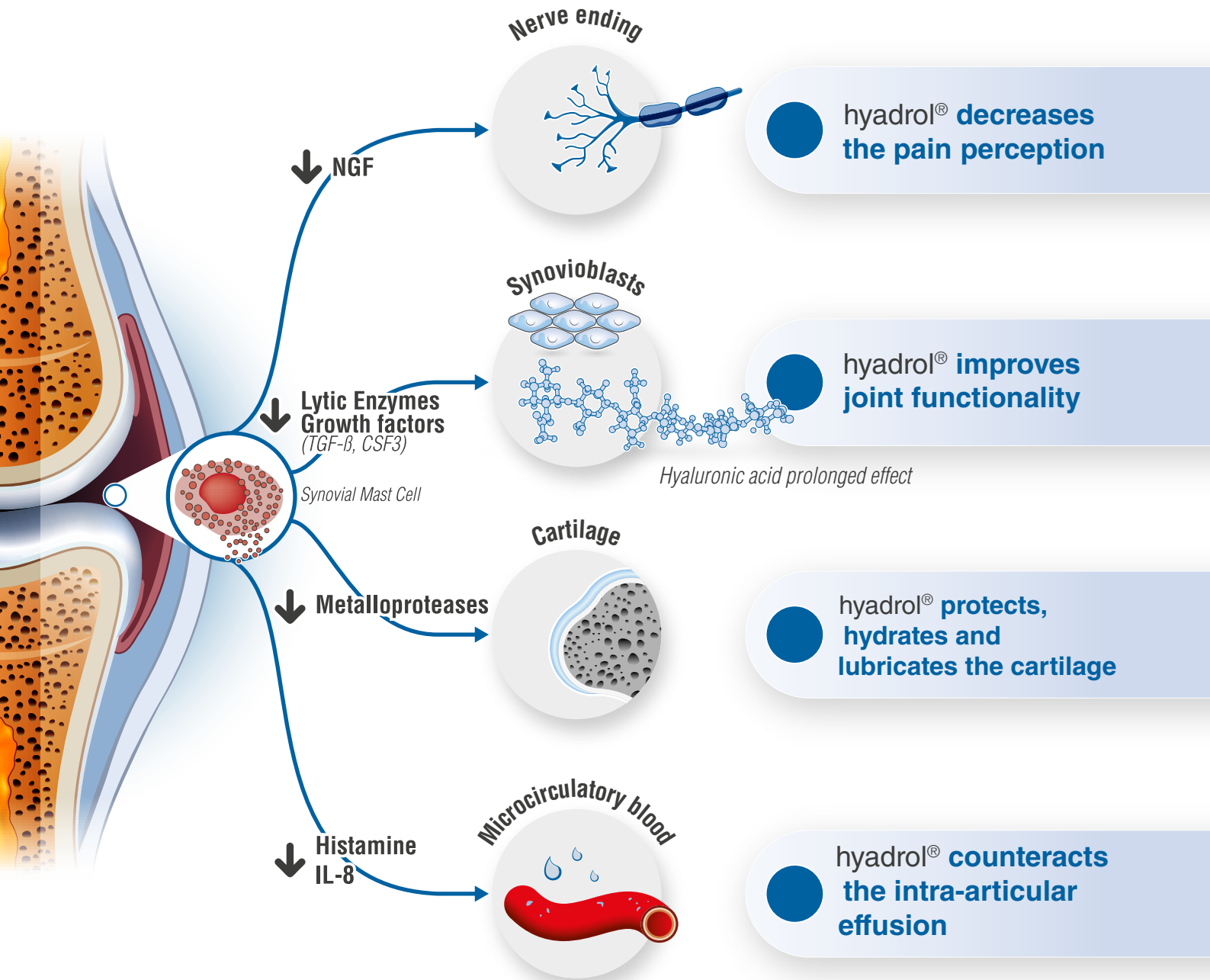
Hyaluronic acid bio-binding epitope*

CD44 receptors interact with only one binding region (blue circle) expressed by hyaluronic acid.

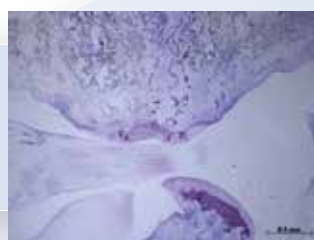


Effect of the hyadrol[®] combination (*Adelmidrol 2% + Hyaluronic acid 1%*) in the cartilage degeneration in an animal model of osteoarthritis⁽⁵⁾

Overall action on the mechanisms sustaining the impaired joint metabolism



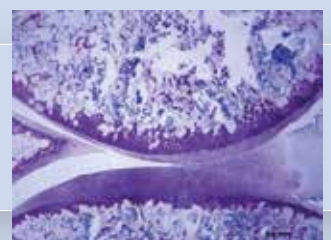
Control



Osteoarthritic joint



Osteoarthritic joint after a treatment with hyaluronic acid (1%)



Osteoarthritic joint after treatment with hyadrol®

Gonarthrosis treatment with intra-articular injections of an association of hyaluronic acid and Adelmidrol (hyadrol®)

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Clinical study

MATERIALS AND METHODS

PATIENTS: 102 patients with Kellgren-Lawrence grade II-III gonarthrosis.

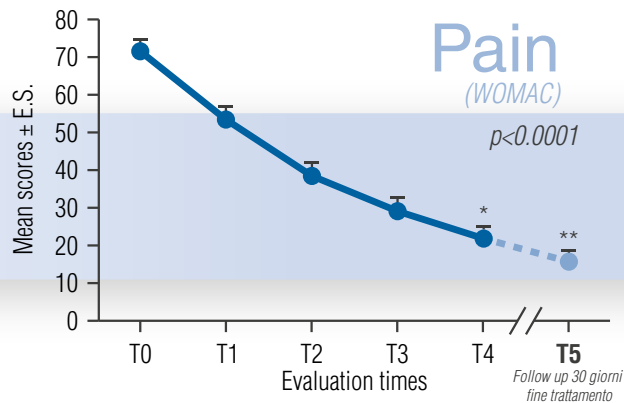
TYPE OF STUDY: open trial

TREATMENT: all patients received once a week for 4 weeks one intra-articular injection with hyadrol® (Adelmidrol 2% and hyaluronic acid 1%).

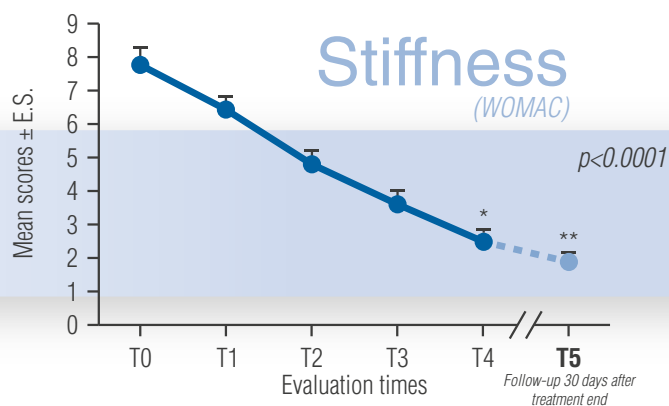
EVALUATION TIME AND METHODS:

- WOMAC scale;
- 12-Item Short Form Health Survey questionnaire (SF-12);
- Likert Patient Global Impression of Change scale (PGIC);
- follow up (T) at 30 days after the end of treatment.

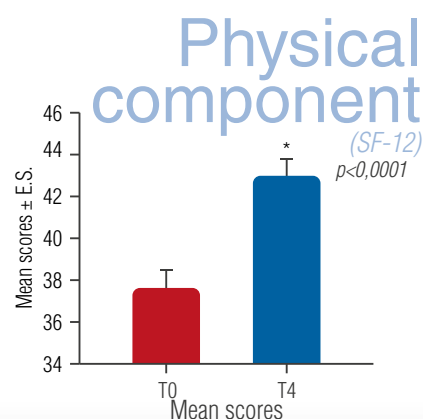
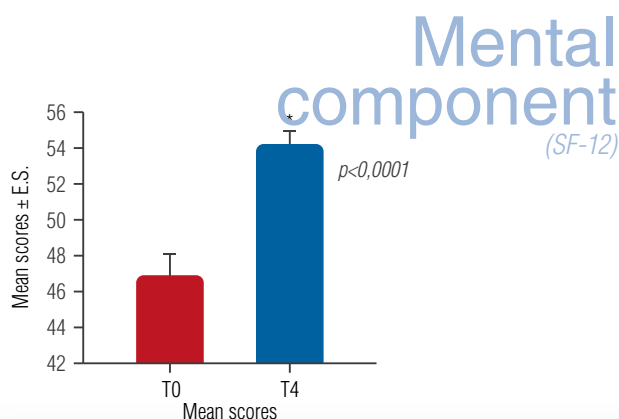
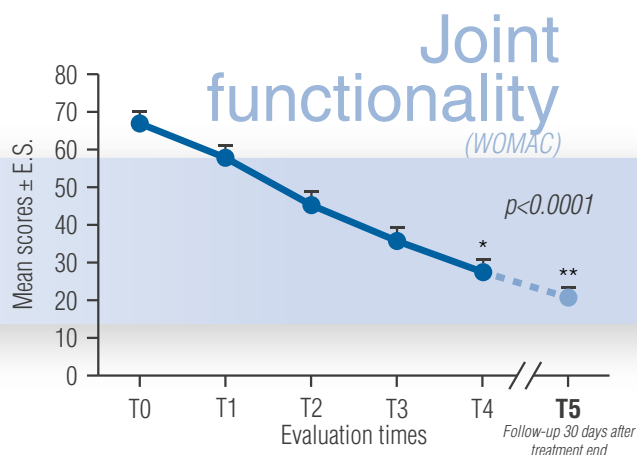
hyadrol[®] **decreases joint pain** intensity



hyadrol[®] **decreases joint stiffness**



hyadrol[®] **improves joint functionality** and the mental component



Highly significant improvement in the mental component of the quality of life at the end of treatment.

Highly significant improvement in the physical component of the quality of life at the end of treatment.



Sterile single-use Medical Device for intra-articular injection

Pre-loaded Syringe 2ml

hyadrol® is a combination of Adelmidrol (2%) and Hyaluronic acid (1%) high molecular weight

Adelmidrol is able to favour, locally, the recovery of endogenous Palmitoilethanolamide physiological level in the synovial liquid, counteracting the mast cell hyperreactivity and related neuro-immune-inflammatory processes. The device contains a high molecular weight Hyaluronic acid epitope (ranging between 1,3 and 2,0 x 10⁶ Dalton) suitable for determining bioadhesion and visco-induction, produced via microbial fermentation; the synthesis occurs in absence of protein matrices and purified of any proteic fractions, to avoid every immune reactions.

INTENDED USE: for the treatment of joint capsule dysmetabolism associated with degenerative arthropathies, with special reference to:

- **Gonarthrosis**
- **Knee Rheumatoid arthritis**

USE: 1 intra-articular injection every 7 days for 5 weeks, unless specified by a doctor. Use an appropriately sized sterile needle (from 19 G to 21 G). hyadrol® it can only be administered by qualified medical staff, in adequate environmental conditions and according to the technical standards required in case of intra-articular injections.

INSTRUCTIONS: special care must be taken in patients with ongoing infections in areas close to the injection sites, to avoid bacterial arthritis onset. It is recommended not to subject the joint to excessive load in the hours immediately following the injection.

PREGNANCY AND LACTATION: no teratogenic phenomena are known. However, it is recommended not to use the device during pregnancy and lactation, unless otherwise judged by a doctor.

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