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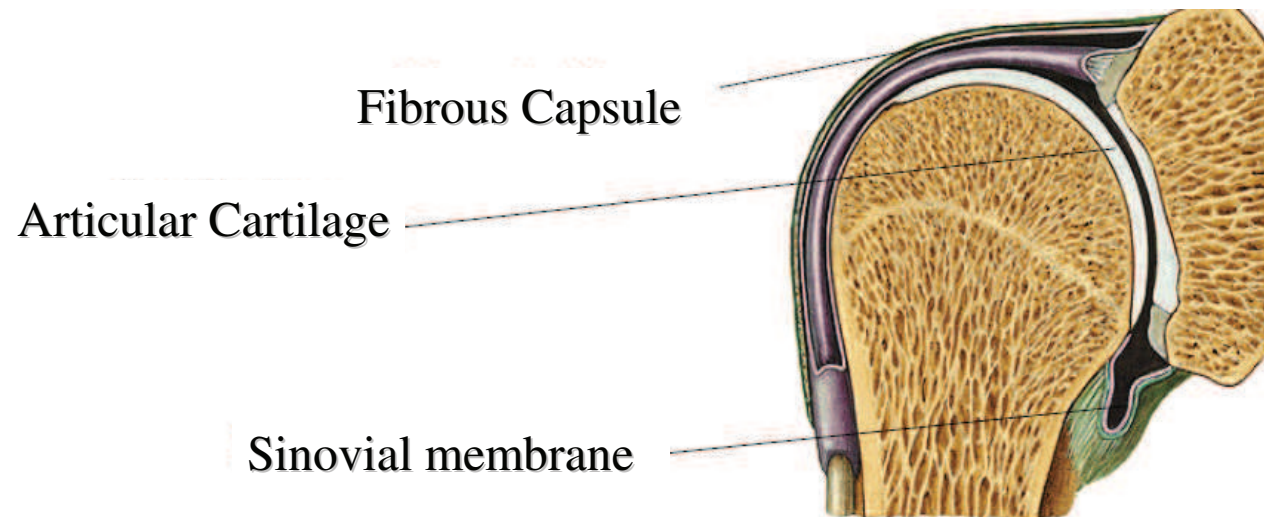
The synovial fluid

composition:

- ialuronan
- water
- ions

properties:

- *high viscosity*
- *colourless liquid*

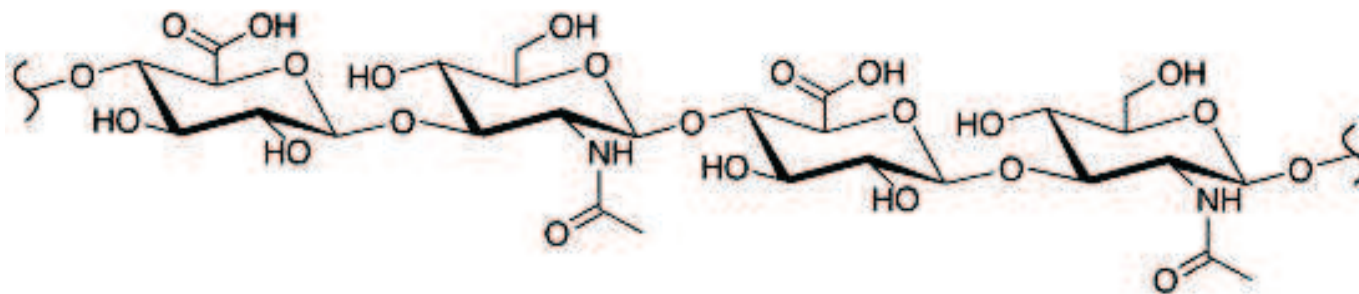


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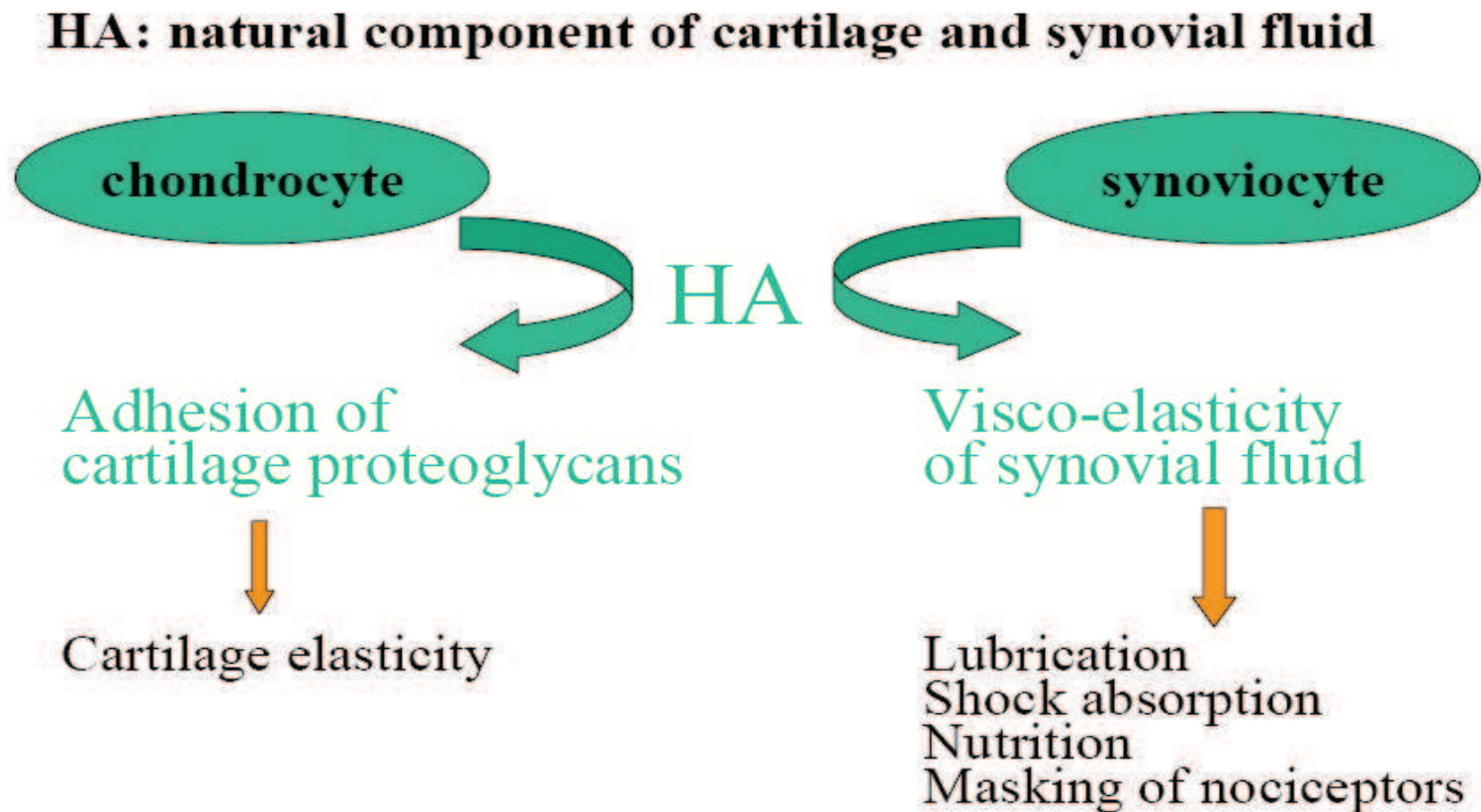
Intraarticular hyaluronic acid:

- **linear**
- **polymer of glucosamine and glucuronic acid**
- **molecular weight $2 \times 10^5 \sim 10^7$ Da**

Hyaluronic Acid



Hyaluronic acid properties



Hyaluronic acid and osteoarthritis (OA)

HA MW and concentration decrease in OA

	Normal	OA
MW (MDa)	> 1	< 1
Concentration (mg/mL)	2-4	< 2
Elasticity	20	8
Viscosity	10	5

 **Cartilage lubrication is not guaranteed**

Hyaluronic therapy guidelines

EXTENDED REPORT

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K M Jordan, N K Arden, M Doherty, B Bannwarth, J W J Bijlsma, P Dieppe, K Gunther, H Hauselmann, G Herrero-Beaumont, P Kaklamanis, S Lohmander, B Leeb, M Lequesne, B Mazieres, E Martin-Mola, K Pavelka, A Pendleton, L Punzi, U Serni, B Swoboda, G Verbruggen, I Zimmerman-Gorska, M Dougados

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Ann Rheum Dis 2003;62:1145-1155. doi: 10.1136/ard.2003.011742

SIR e LIMAR

Consensus Italiana sulle raccomandazioni dell'EULAR 2003 per il trattamento dell'artrosi del ginocchio.

Reumatismo 2004;56(3):190-201

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OA: therapeutical options

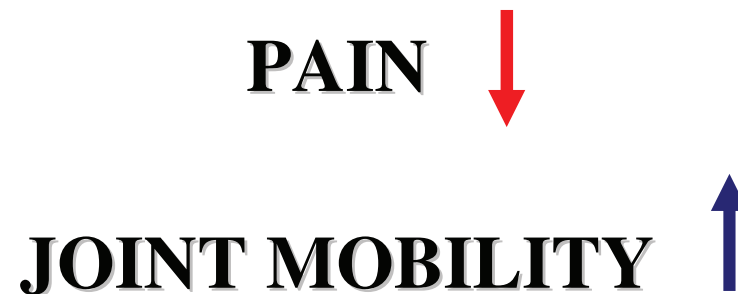
Table 1 Treatment modalities identified for the treatment of knee OA

Non-pharmacological	Pharmacological	Intra-articular	Surgical
Education	Paracetamol	Corticosteroid	Arthroscopy
Exercise	NSAIDs	Hyaluronic acid	Osteotomy
Insoles	Opioid analgesics	Tidal irrigation	UKR
Orthotic devices	Sex hormones		TKR
Weight loss	SYSADOA		
Laser	Psychotropic drugs		
Spa	Topical NSAID		
Telephone	Topical capsaicin		
Vitamins/minerals			
Pulsed EMF			
Ultrasound			
TENS			
Acupuncture			
Nutrients			
Herbal remedies			

EMF, electromagnetic field therapy; TENS, transcutaneous electrical nerve stimulation; NSAIDs, non-steroidal anti-inflammatory drugs; SYSADOA, SYmptomatic Slow Acting Drugs for OA (includes avocado/soybean unsaponifiables (ASU), chondroitin, diacerein and glucosamine); UKR, unicompartmental knee replacement; TKR, total knee replacement.

Mechanism of action of HA injections in OA joint

- **Mechanic action**
- **Analgesic action**
- **Anabolic action**



Tolerability of HA

- Pain at the injection site
- Moderate inflammatory reactions
- Articular effusion
- Infection
- Pseudogout crises (CCA)
- Hypersensitivity/Allergy (*aviary origin*)
- Pseudosepsis (*hylan*)
- Granulomatous reactions (*hylan*)

depending on injection technique, possibly product related (MW, concentration)

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Product profile:

- Medical device – class III
- HA from biofermentative origin (*no animal protein*)
- up to 2% native HA (*no chemically modified*)
- molecular weight 1,000,000 Da
- filling volume up to 3 ml
- ready to use syringe
- Luer-lock
- Steam sterilization



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Presentation:

sterile physiologic solution of HA (sodium salt) in prefilled glass syringes, for intra-articular injections

Indications:

substitute of synovial fluid into joints affected by degenerative or mechanical OA that gives pain or reduced mobility

Dosage:

3 to 5 weekly injections, 2 therapies per year

Side effects:

transitory reactions such as pain, rigidity, reddening or swelling, that usually disappear rapidly

Mechanism of action of HA injections in OA joint

1. Mechanic action:

- shock absorber
- lubrication
- cartilage elasticity



Mechanism of action of HA injections in OA joint

2. Anti-inflammatory action:

- Inhibition of polynucleated WBC chemotaxis**
- PGE2 synthesis reduction, free-radicals scavenging**
- Inhibition of IL-1 and metalloproteases**

(in human: Todesco 1992, Hirota 1998, Punzi 2000)

Mechanism of action of HA injections in OA joint

3. Analgesic action

- Reduction of sensitivity of mecano-nociceptors ionic channels (*Pena 2002*)
- covering of pain receptors (« coating » effect)

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Medical device class III **CE** 0373