Hyaluronic acid has been used for almost thirty years for the relief of osteoarthritis, but we could not understand how it worked.

It could be found after administration for only few hours and even its viscosity was too low. In spite of all this it was found to have long-lasting effect in osteoarthritic joints.

Recent research has highlighted that high molecular weight hyaluronic acid (HMWHA) has three separate and synergic actions in the joint:

- **Lubrication effect**
- **Disease modifying effect**
- **Analgesic effect**

**LUBRICATION EFFECT**

HA is able to bind with surface-active phospholipids exerting a lubricating action much higher that its inherent viscosity would allow.

**CONCLUSIONS & INTERPRETATION**

**VOLUME**

- Cartilage
- Synovial fluid
- Lipid-multilayer (2:7 bilayers)

- Discontinuous structure of synovial liquid
- Lipid multilayers
- Sliding location between lipid bilayers
- cT = 0.008

**INTERFACIAL FILM**

- Hyaluronic acid + seric proteins

**ANALGESIC EFFECT**

Joint pain takes place through stretch-activated ion channels, which open in response to increased membrane tension. A study has demonstrated that only HMWHA is able to reduce the sensitivity of ion-channel of nerve pain terminals. The Low Molecular Weight one was ineffective.

**DISEASE MODIFYING EFFECT**

HMWHA is able to reduce MMP-2 and MMP-9, TNF-α, Aggrescanase-2, IL-8 and NO all enzymes responsible for the degradation of cartilage and the progress from osteoarthritis to osteoarthrosis.

Furthermore HMWHA is able to reduce these enzymes for significantly longer than Low molecular weight HA.

**Duration of reduction of cytokines in hours**

- **LMWHA**
  - 24

- **HMWHA**
  - 96

Furthermore Gomis et al. compared three different commercial preparations of HA to evaluate their respective analgesic properties after a single injection in normal and acutely inflamed rat joints. The analgesic properties of HA where in direct relationship with their molecular weight whereas the LMW HA did not have analgesic effect nor in normal nor in inflamed joints. The HMW HA had a prolonged and significant analgesic effect in both joints reducing input discharge by 50% on average. In this study the medium-weight HA had some effect, but of limited duration and only in the inflamed joint.
MOLECULAR WEIGHT OF COMMON PRODUCTS

<table>
<thead>
<tr>
<th>Product</th>
<th>Conc. (mg/ml)</th>
<th>Molecular weight (Dalton)</th>
<th>Recommended dose</th>
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</thead>
<tbody>
<tr>
<td>Hyaluronan</td>
<td>10</td>
<td>0.7 x 10^6</td>
<td>20 mg</td>
</tr>
<tr>
<td>Map-5*</td>
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<td>0.76 x 10^6</td>
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<td>Hylasac</td>
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<tr>
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<tr>
<td>Synacred</td>
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<td>0.15 x 10^6</td>
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<tr>
<td>Equitex</td>
<td>5</td>
<td>1 x 10^6</td>
<td>10 mg</td>
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<tr>
<td>Legam/6</td>
<td>10</td>
<td>0.26 x 10^6</td>
<td>40 mg</td>
</tr>
</tbody>
</table>

*Not registered for intra articular use

TAKE HOME MESSAGE

- **High Molecular Weight Hyaluronic Acid has a lubricating effect in non-inflamed joints;**
- **High Molecular Weight HA exerts prolonged Disease Modifying activity in joints;**
- **High Molecular Weight HA reduces joint pain by 50%;**

REFERENCES


Hyvico your weapon against joint dysfunction

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