An innovative non-animal chitosan hydrogel is able to restore the rheology of osteoarthritis synovial fluid ex vivo

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Purpose
To evaluate ex vivo the ability of an innovative chitosan hydrogel to improve the rheological properties of synovial fluid that was collected from osteoarthritic knee.

Materials
Chitosan and hyaluronic acid (HA) viscosupplements:
- Chitosan hydrogel SYN011 (KiOmed Pharma), made of non-animal ultrapure chitosan using a proprietary crosslinking-free technology
- Commercial HA viscosupplements
  - Crosslinked HA: Hylan G-F-20 (Synvisc-One®, Sanofi-Aventis)
  - Non crosslinked HA: Ostenil Plus (TRB-Chemedica)

Osteoarthritic synovial fluids (OASF), collected from 20 patients (51-73 year-old) before undergoing total knee replacement and stored at -20°C until analysis

Methods
- OASF samples were mixed with SYN011 or HA at 1:1 ratio (v/v) (N=10 for each product), and the mix was incubated 2 hours at 37°C prior to rheology (Figure 1)
- Rheology tests were performed by using a calibrated HR-2 rheometer (TA instruments) at 37°C. Measured parameters were:
  - G’ (characterizes the elastic behavior)
  - G” (characterizes the viscous character)
  - G’/G” crossover frequency
  - tan δ
- These parameters were measured at steady state (0.01 rad/s), walk frequency (3.98 rad/s) and run frequency (25.1 rad/s) in the frequency sweep mode. Zero-shear viscosity (viscosity at rest) was measured at a frequency of 0.006 s⁻¹.

Results
Viscosupplements. SYN011 alone expressed three important rheological properties for its use as viscosupplement: it could simultaneously exhibit gel character (tan δ<1), high elasticity and high viscosity at rest.

Impact of OA on the synovial fluid. The synovial fluid was significantly impacted by the joint pathological status, resulting in loss of gel character (tan δ>1) and decrease of elasticity (Table 1).

Supplementation of OASF. When mixed with OASF at a 1:1 (v/v) ratio, only SYN011 and Hylan G-F 20 were able to restore the gel character of OASF up to the level of healthy synovial fluid below walk frequencies, with G’/G” crossover and tan δ below 1. In comparison to OASF mixed with Hylan G-F-20, OASF mixed with SYN011 showed a significantly higher viscosity, while G’ was in a similar range.

Conclusion
SYN011, an innovative non crosslinked chitosan hydrogel, is able to fully restore the rheological function of the synovial fluid of patients suffering from osteoarthritis, up to the level of healthy synovial fluid. In addition, its lubrication capacity is significantly higher than that of a crosslinked hyaluronic viscosupplement. These results indicate that chitosan hydrogel SYN011 is a good candidate for intra-articular treatment of OA.

Reference