

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 hyaluronan (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-Chemica)

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 hyaluronan viscosupplement**. These results indicate that chitosan hydrogel SYN011 is a good candidate for intra-articular treatment of OA.

Reference

[1] Bhuanantanondh et al. 2010. "Rheological Study of Viscosupplements and Synovial Fluid in Patients with Osteoarthritis." J Med Biol Eng 32 (1): 12–16.

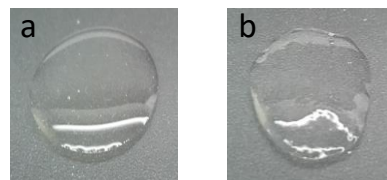


Figure 1. OASF alone (a) and OASF mixed with SYN011 chitosan gel (b). The OASF/SYN011 mix is visibly more cohesive than OASF alone. SYN011 and OASF showed good compatibility (no clumping, no precipitation).

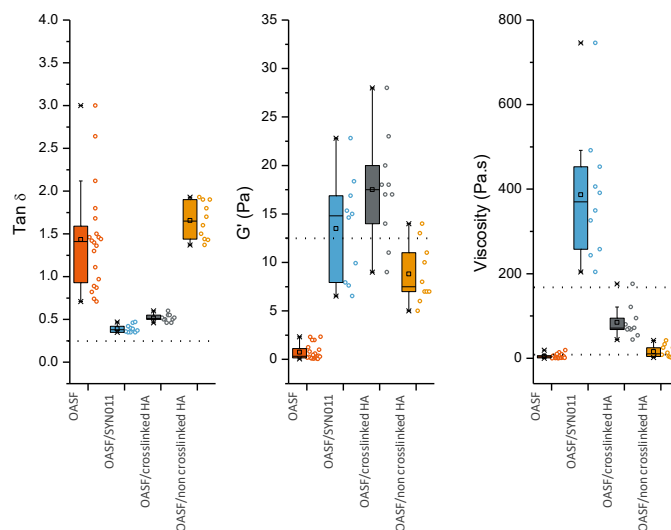


Figure 2. Box plot showing the rheology of OASF alone and OASF supplemented with SYN011 chitosan gel, crosslinked HA (Hylan G-F-20) and non crosslinked HA (Ostenil Plus). --- Values for healthy synovial fluid [1].

Formulation	Tan (δ) at walk frequency	G'/G'' crossover frequency (rad/s)	G' at walk frequency (Pa)	Zero shear viscosity (Pa.s)
Healthy synovial fluid [1]	0.25	0.06 – 0.15	12	6 - 175
OASF	1.4 ± 0.6	0.1 – no crossover	0.7 ± 0.8	5 ± 5
OASF - SYN011	0.4 ± 0.1	< 0.1	13.5 ± 5.3	387 ± 157
OASF – crosslinked HA	0.5 ± 0.1	0.7 – 0.4	17.5 ± 5.5	85 ± 38
OASF – non crosslinked HA	1.7 ± 0.2	0.7 – no crossover	8.8 ± 3.0	16 ± 14

Table 1. Rheology of OASF alone and OASF supplemented with SYN011 chitosan gel, crosslinked HA (Hylan GF-20) and non crosslinked HA (Ostenil Plus) (average ± standard deviation).