

# AN INNOVATIVE HYALURONIC ACID PRODUCT FOR VISCOSUPPLEMENTATION IN PATIENTS WITH OSTEOARTHRITIS



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## Background

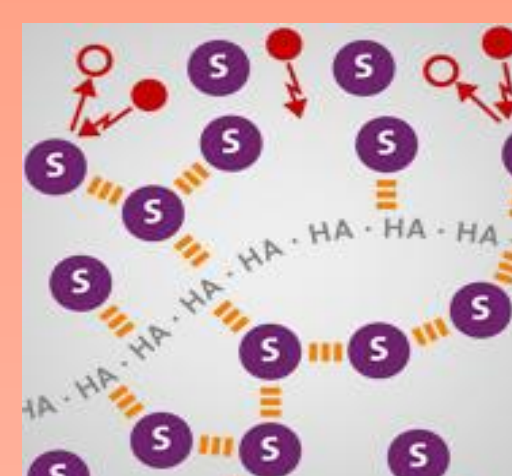
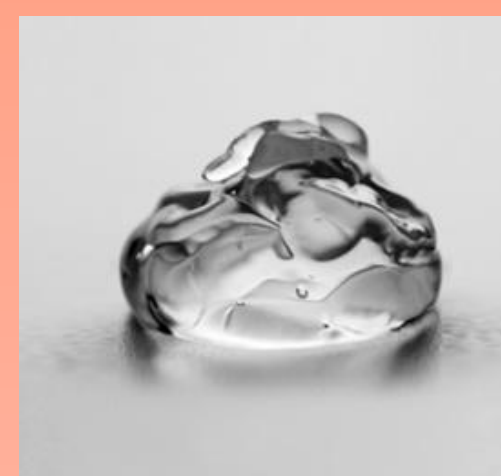
Osteoarthritis (OA) is a very common joint disorder and its prevalence is increasing. It is projected that by the year 2030, almost 67 million US adults will have been diagnosed with arthritis [1].

Viscosupplementation (VS) is used for more than 20 years and is recommended in the treatment of OA. There are currently more than 20 commercial VS products available worldwide. These products differ in hyaluronic acid (HA) origin, HA concentration, HA molecular weight, HA chemical modification, rheological properties, dosing regimens, claims of safety and efficacy and residence time into the joint.

Synolis® V-A (Anteis SA) is an innovative VS launched on the market in 2010. The patented [HA+sorbitol] formulation of this VS is based on a high molecular weight of HA (> 2 MDa in the final sterilized gel) from non animal origin, with a high HA concentration (20 mg/ml), combined with a high concentration of a free radical scavenger, the sorbitol (40 mg/ml).

## Purpose

The aims of this study are to evaluate the rheological properties and the resistance to free radicals degradation of Synolis® V-A



## Method

The rheological properties (elastic and viscous moduli :  $G'$  and  $G''$ ) of Synolis® V-A are measured by frequency sweep experiments at 25°C thanks to an AR2000 rheometer (TA Instruments), using a plate and plate geometry with 1 mm gap.

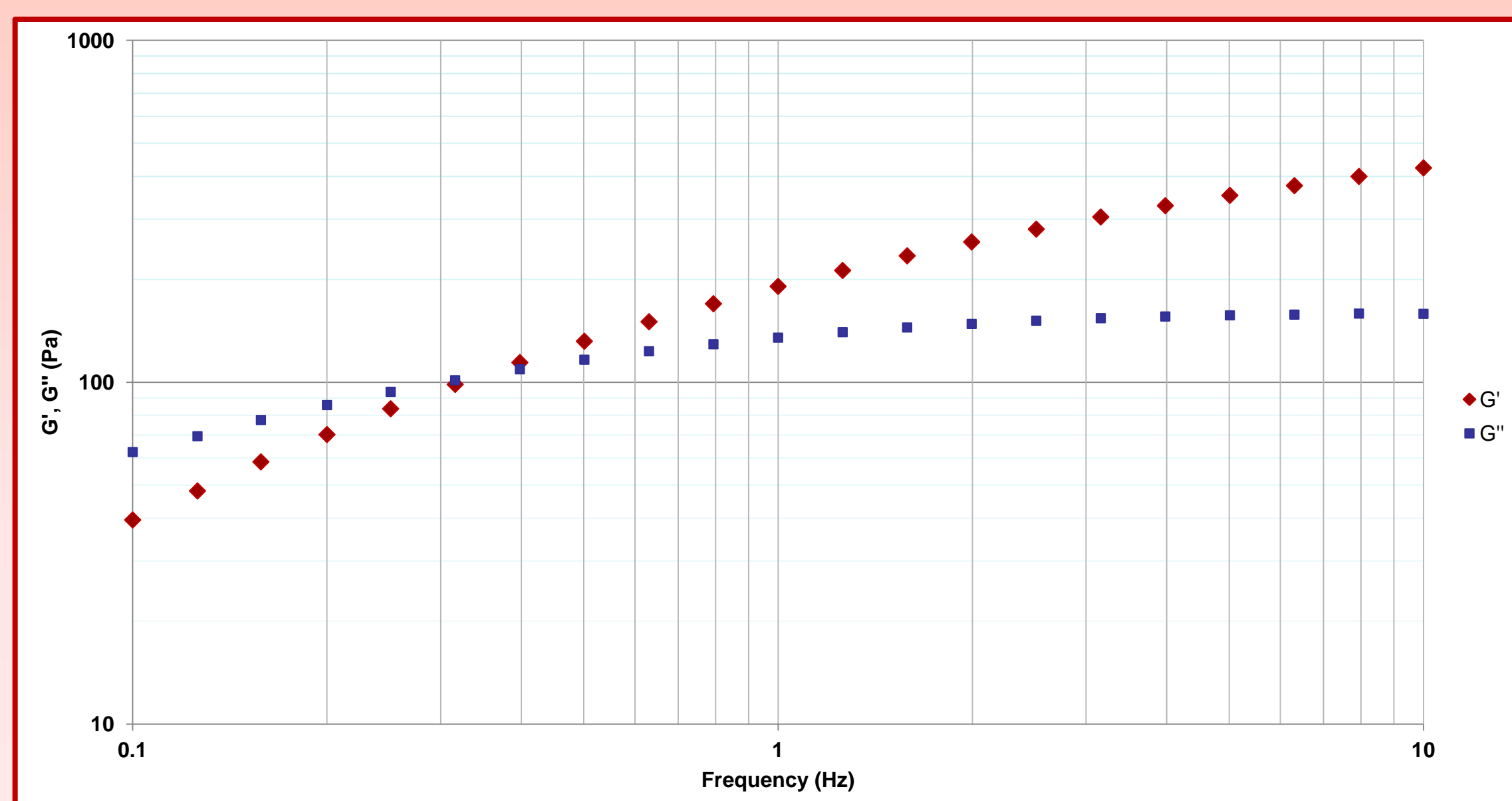
The resistance to free radical degradation of Synolis® V-A is measured with 2 different tests and the results are compared with other VS of the market:

- Test 1 (visual observation): addition of an oxidant agent ( $H_2O_2$ ) on the tested VS (weight of  $H_2O_2 = 1/15 \times$  Weight of VS) followed by the heating of the mixture at 60°C in order to accelerate the oxidative reaction. A visual observation of the flow is performed over time.

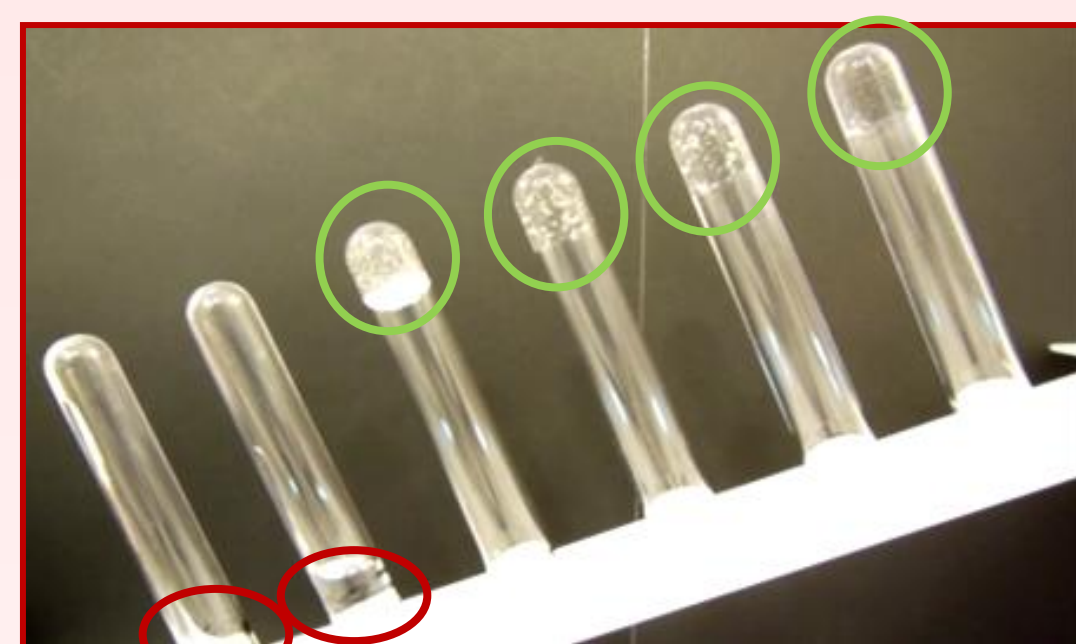
-Test 2 (rheological test): addition of an oxidant agent ( $H_2O_2$ ) on the tested VS (weight of  $H_2O_2 = 1/15 \times$  Weight of VS) and measurement of the rheological properties by time sweep experiments at 37°C thanks to an AR2000 rheometer (TA Instruments), using a plate and plate geometry with 1 mm gap.

## Results

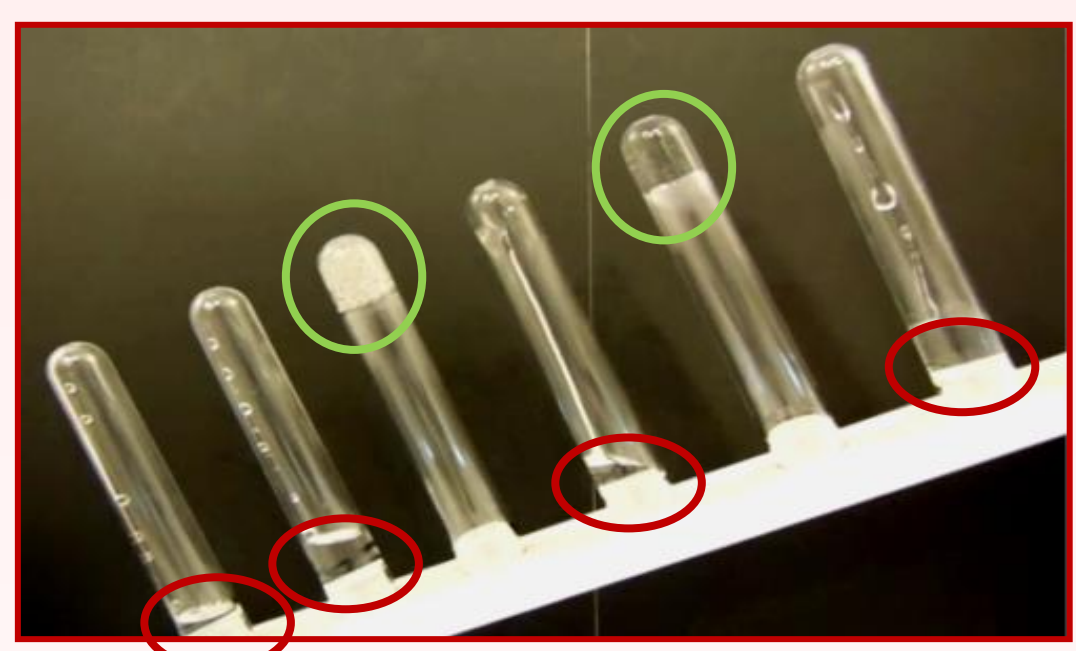
### Rheological properties of Synolis® V-A



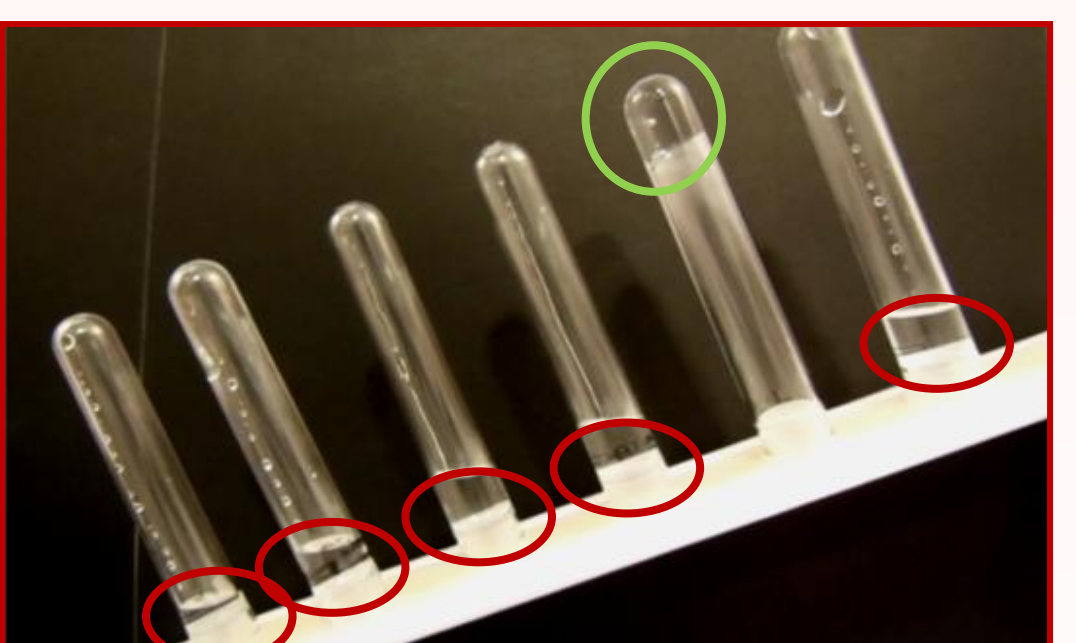
### Resistance to free radical degradation of Synolis® V-A and other products of the market



Before Heating



After 1h at 60°C



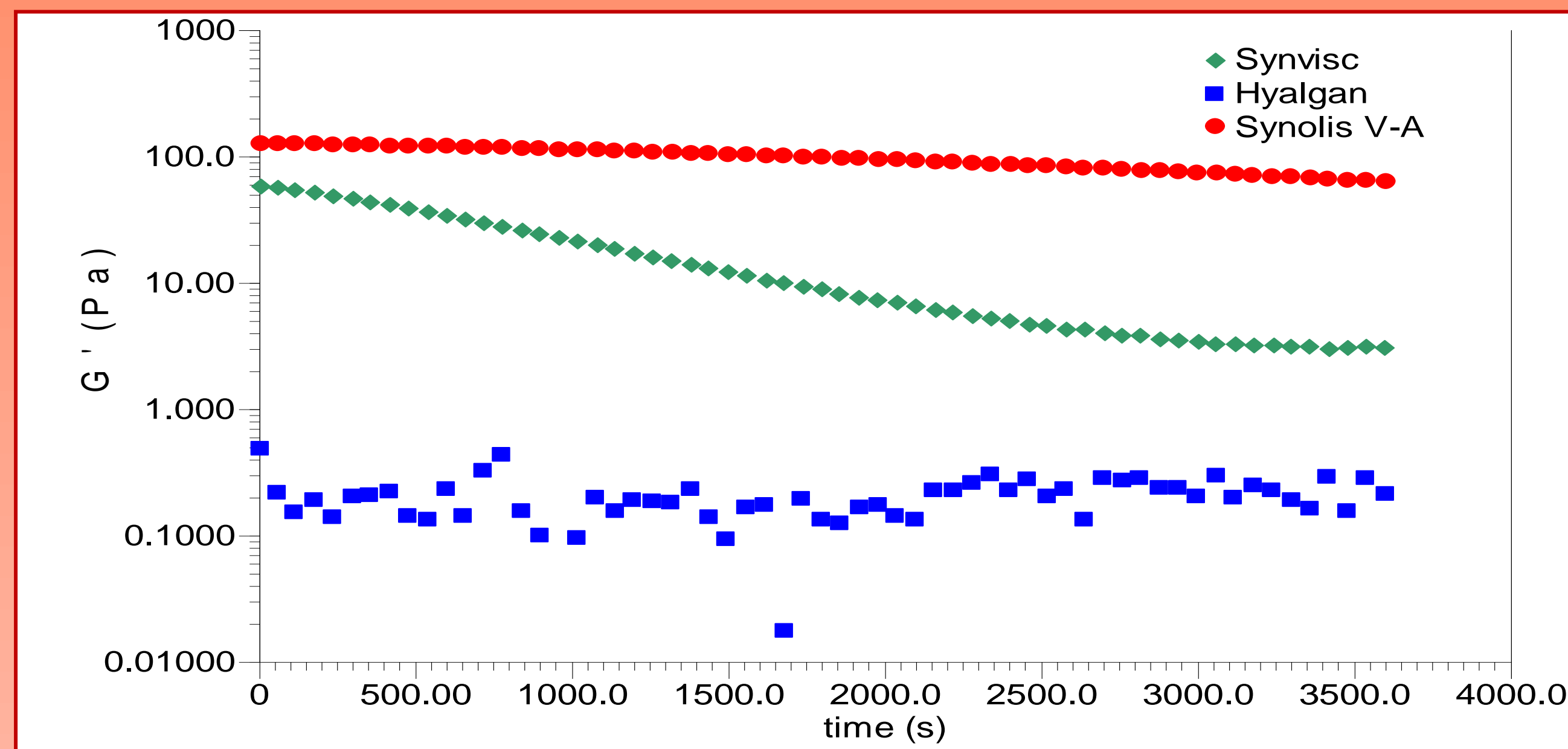
After 3h at 60°C

Tubes:

- 1 – Sinovial®
- 2 – Hyalgan®
- 3 – Durolane®
- 4 – Ostenil® Plus
- 5 – Synolis® V-A
- 6 - Synvisc®

## Test 2:

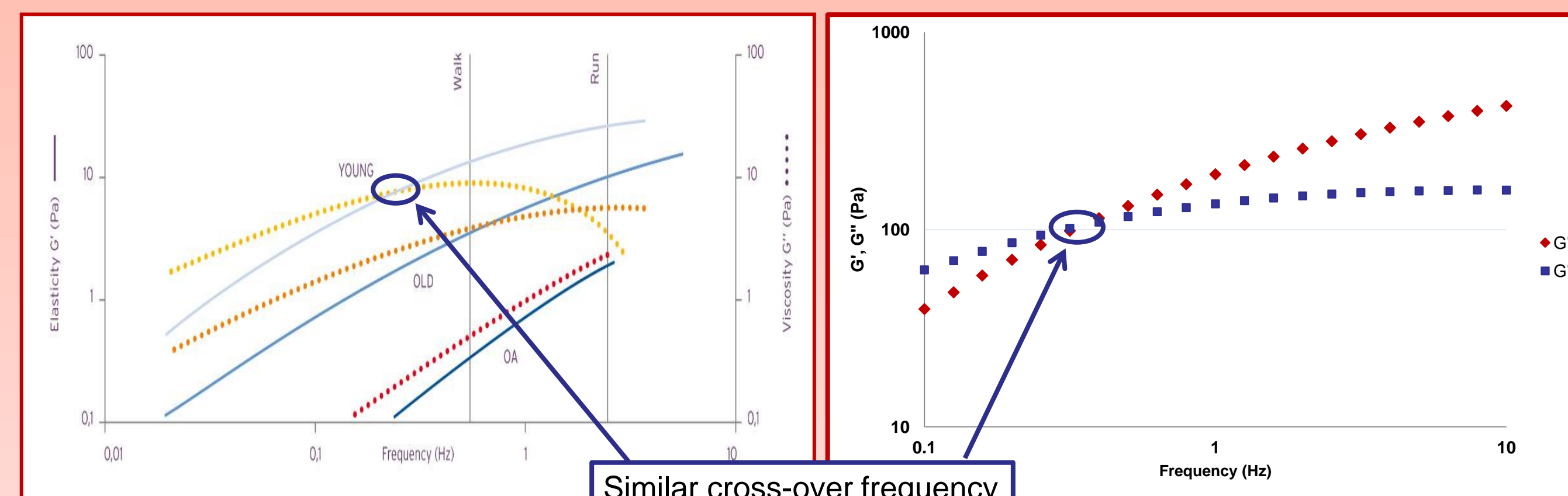
Measurement by rheology of the resistance to free radical degradation



## Discussion

### Rheological properties of Synolis® V-A

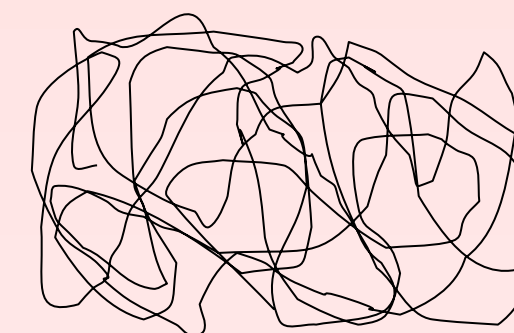
The rheological analysis of Synolis® V-A shows that this VS is characterized by a visco-elastic behavior close to the synovial fluid (viscous and elastic moduli crossing at about 0.4 Hz, as with the healthy synovial fluid) [2-3].



Thanks to this specific frequency crossover, Synolis® V-A mimics the rheological properties of the healthy synovial fluid:

- for a high frequency ( $f > 0.4$  Hz / strong stress exerted in the joint : running, jumping), the elastic modulus of the VS is higher than the viscous modulus: there is a strong protection of the joint by absorption of the produced energy.

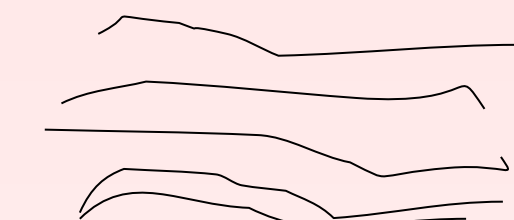
Synolis V-A response to strong mechanical stress (same as synovial fluid)



High elasticity of the VS : Shock absorption in the joint

- on the contrary, for a low frequency ( $f < 0.4$  Hz / weak stress exerted in the joint: resting), the viscous modulus of the VS is higher than the elastic modulus: there is a good lubrication of the joint.

Synolis V-A response to weak mechanical stress (same as synovial fluid)



High viscosity of the VS : Lubrication of the joint

Moreover, due to the high affinity between HA and sorbitol, the structure of Synolis® V-A is stabilized through a very dense network of hydrogen bonds. This complex structure of gel presents remarkably high visco-elastic properties, even higher than animal or crosslinked products. It allows Synolis® V-A to have a very high capacity to lubricate and absorb the shock in the joint.

### Resistance to free radical degradation of Synolis® V-A and other products of the market

According to the literature [4-8], the free radical degradation is a key factor of the HA resorption in the joint and is an important factor of the OA.

Synolis® V-A was designed to have a high capacity to scavenge and neutralize free radicals (= antioxidant effect) thanks to its unique [HA / sorbitol] combination (high ability of the sorbitol to scavenge the free radicals).

As demonstrated by 2 different in vitro tests, Synolis® V-A presents a high capacity to resist to free radicals, better than all the other studied VS. This advantage is key to maintain the Synolis® V-A formulation and its specific rheological properties longer in the joint.

## Conclusion

Synolis® V-A is an innovative viscosupplement made of a combination of HA and sorbitol. Due to its patented formulation and manufacturing process, Synolis® V-A has outstanding rheological properties and a high resistance against *in vivo* degradation in the joint.

As demonstrated by several experiments described in this study, Synolis® V-A is characterized by:

- a visco-elastic behaviour close to the human synovial fluid and a very high elasticity and viscosity to have a VS with a high capacity to lubricate the joint and to absorb shocks, as with a healthy synovial fluid
- a high capacity to scavenge and neutralize free radicals, which allows to maintain the VS longer in the joint, for better clinical outcomes.

## References:

- 1 – Altman RD, Pain, osteoarthritis, and intra-articular HA...Today and beyond, OA pain management update, Special report, 2007; 2 – Mazzucco D, McKinley G, Scott RD, Spector M, Rheology of joint fluid in total knee arthroplasty patients, J Orthop Res, 2002 Nov;20(6):1157-63.; 3 – Fam H, Bryant JT, Kontopoulou M, Rheological properties of synovial fluids, Biorheology, 2007;44(2):59-74; 4 – Henrotin Y, Kurz B, Antioxidant to treat osteoarthritis: dream or reality?, Curr Drug Targets, 2007 Feb;8(2):347-57; 5 – Fermor B, Christensen SE, Youn I, Cernanec JM, Davies CM, Weinberg JB. Oxygen, nitric oxide and articular cartilage, Eur Cell Mater, 2007;13:56-65.; 6 – Saari H, Oxygen derived free radicals and synovial fluid hyaluronate, Ann Rheum Dis, 1991 Jun;50(6):389-92.; 7 – Lunec J, Halloran SP, White AG, Dormandy TL, Free-radical oxidation (peroxidation) products in serum and synovial fluid in rheumatoid arthritis, J Rheumatol, 1981 Mar;8(2):233-45.; 8 – Zoskoven C, Jäger M, Zilkens C, Bloch W, Brixius K, Krauspe R, Oxidative stress in secondary osteoarthritis: from cartilage destruction to clinical presentation?, Orthopaedic Reviews, 2010, volume 2:e23