RESILIENT HYALURONIC ACID™

PATENTED TECHNOLOGY

REFERENCES

5- Bourdon F., Charton E., "Lift Capabilities evaluation of Hyaluronic Acid fillers", Poster presentation AMWC Monaco 2012.
OBJECTIVE

This in vitro study evaluates the sensitivity to bovine hyaluronidase (HAase) of 6 commercially available hyaluronic acid (HA) – based dermal fillers. A correlation has been established between the gel’s resistance to HAase, and the gel’s resistance to compression, i.e. its cohesivity. Results obtained are good indicators to assess the best candidates for long-lasting capabilities products.

INTRODUCTION

HA-based dermal fillers are non-permanent implants that will degrade in vivo via complex mechanisms including free radicals and HAase. The resistance of the gels against such degradation could be linked to their intrinsic mechanical properties. However, there is no study so far that demonstrates this relationship. Besides, the methods described in the literature to characterize the in vitro sensitivities of HA gels to HAase are generally non-direct, and consist in assaying the fragments of HA released upon HAase action. We describe here a simple and intuitive test, based on the effect of the degradation on the gel’s mechanical properties. This new method resides in measuring the decrease of the gel G’ (elastic modulus measured in oscillatory rheology) after incubation with a precise dose of HAase during a limited time. The decrease of G’ can be linked to the decline of the lift capabilities, when the gel is being degraded in vivo. It is to be noticed that the dose of HAase used for the present test is about 50 times lower than the dose possibly used for a therapeutic action, i.e. treatment of overcorrection or rare complications. With such “therapeutic dose”, all the dermal fillers of this study are totally degraded.

MATERIAL AND METHODS

The fillers were obtained from commercial sources. A same batch of product was used for all the tests before expiry date.

HAase degradation

100µL of a solution of HAase (from bovine testicular, type IV/S, Sigma), prepared at 16U/mL in H2O, is added to 3g of the tested HA gel Mass. Thus the global activity of HAase is 0,5µU/g of gel, which represents globally 1,5U HAase in each sample. The resulting mixture is homogenized and incubated 24 hours at 37°C, then immediately cooled at 25°C for rheology measurement.

Rheology: Dynamic oscillatory test

Each sample is tested before and after incubation with HAase, with the following protocol: measurements at 25°C and 1Hz angular frequency, with amplitude sweep corresponding to an applied deformation strain from 1 to 1400 Pa, using a Thermo Haake RS3000 rheometer with a 35mm / 1° Titanium cone-plate geometry. The resulting stress response is measured: G’ and G” are recorded at low strain (i.e. 5Pa), i.e. almost at rest.

Compression test

2.5 g of gel are placed between the 2 plates of 35mm plane-plane geometry, using a Thermo Haake RS3000 rheometer. The rheometer is set to a normal force mode: the upper plate is put in contact with the gel and is lowered toward the bottom plate, thus compressing the gel. The course is stopped when a 70% compression rate is reached. The resulting normal force is measured and integrated during the experiment, from 0 to 70% compression rate, which leads to the resistance to compression (N).

RESULTS AND DISCUSSION

Figure 1 shows the G’ values measured for the HA gel fillers before and after incubation with HAase.

Elastic modulus G’ is a measure of the energy which is stored by the gel and returned when the gel is subjected to small deformations in oscillatory rheology: it represents the hardness of the gel at rest. The G’ values of the HA gel fillers tested are quite different. But in all cases, the incubation with HAase results in a decrease of the G’ values, which demonstrates the degradation of the gels due to the enzyme (figure 1). Thus, we assess the resistance to HAase as the % of the initial G’ remaining after degradation. The fillers usually described as “particulate gels” (Restylane® L and Perlane® L) show the highest G’ values in this dataset, but we observe a significant degradation of these fillers after incubation with HAase (respectively 25% and 39% of the initial G’ value remained after degradation). In opposition, the decrease of G’ after incubation is lower for the Juvederm® products (56% and 69% of initial G’ remained), and far lower for Teosyal® products (81% and 89% of initial G’ remained).

We represent hereunder the resistance to HAase as a function of the initial G’ value (figure 2), and as a function of the cohesivity of the tested products (figure 3):

CONCLUSION

The last capabilities are essential for a dermal filler to ensure an optimal and regular aesthetic result throughout the lifetime of the implant. A higher resistance to degradation enables to maintain the mechanical properties of the implant over time, and thus to offer better Lasting Capabilities.

The measurement of the decrease of G’ after incubation of the gel with HAase is an intuitive method that leads to the direct analysis of the dermal filler resistance to degradation. This is an in vitro and not an in vivo study, which means that the real longevity needs to be confirmed with clinical results.

We demonstrated in this in vitro study a correlation between the gel’s resistance to flattening, i.e. its cohesivity, and the gel’s resistance to HAase. Thus, the cohesivity of the gels (measured by their resistance to compression) appears to be an essential factor in the dermal filler lasting capabilities.

Teosyal® PureSense Deep Lines and Ultra Deep are the most cohesive gels among the dermal fillers presently tested. They offer in vitro a better resistance to HAase degradation, and thus better mechanical performances over time. These fillers are intended for the filling of deep wrinkles and the restoring of the face volumes. For such indications, these Teosyal® fillers show optimal lasting capabilities, in order to ensure longer aesthetic results.

REFERENCES

5- Bourdon F., Charton E., Meunier S., “Last capabilities evaluation of Hyaluronic Acid Fillers”, Poster presentation ARMC Monaco 2012.

Corresponding author: s.meunier@teoxane.com

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