LABORATORY SCIENCE

Mixed polymeric systems: New ophthalmic viscosurgical device created by mixing commercially available devices

Daniele Tognetto, MD, Paolo Cecchini, MD, PhD, Rossella D'Aloisio, MD, Romano Lapasin, MEng

Purpose: To evaluate the rheological properties of mixtures of different commercially available ophthalmic viscosurgical devices (OVDs) containing sodium hyaluronate and chondroitin sulfate.

Setting: Eye Clinic, University of Trieste, Trieste, Italy.

Design: Laboratory study.

Methods: Blends were obtained combining a superviscous cohesive OVD (Healon GV [sodium hyaluronate 1%]) and a medium-viscosity dispersive OVD (Viscoat [sodium hyaluronate 3.0%–chondroitin sulfate 4.0%]). The 2 substances were combined in different ratios, and the rheological characteristics were analyzed to find the optimum proportion. A new viscous dispersive OVD, Discovisc (hyaluronic acid 1.6%–chondroitin sulfate 4.0%) was evaluated for comparison. The storage modulus, loss modulus, crossover point, complex viscosity, shear viscosity, and pseudoplasticity were studied.

Results: The rheological properties of the mixed solution (1:1 and 3:1) showed intermediate characteristics in comparison with the 2 original substances, characterized by a viscosity comparable to that of the superviscous cohesive OVD, but at a higher shear rate (similar to the medium-viscosity dispersive OVD). The new viscous dispersive OVD performed similarly to the medium-viscosity dispersive OVD at low shear rates but was comparable to the superviscous cohesive OVD at high shear rates.

Conclusions: The mixture of dispersive and cohesive rheological properties in a single OVD might be an advantage during cataract surgery.

J Cataract Refract Surg 2017; 43:109–114 © 2016 ASCRS and ESCRS

The use of ophthalmic viscosurgical devices (OVDs)[1] in modern ophthalmic surgery is essential.[2–4] During cataract extraction, the use of OVDs makes the surgical procedure safer and easier.[2–5] The ideal OVD should play 2 main roles; that is, space maintenance and tissue protection[2–6] from the surgical instruments and from the insertion of the intraocular lens (IOL).[2–5]

An OVD is required to maintain a deep anterior chamber,[5,7] facilitating a precise and controlled capsulorhexis[8] to allow uneventful IOL implantation,[2,3,8] and to be easily injected and removed from the eye.[8] Ophthalmic viscosurgical devices are essential in dealing with intraoperative complications, providing an adequate workspace for the surgeon,[5,9] manipulating tissues, and acting as a soft spatula.[1,10–13] The protection of the delicate corneal endothelium during surgery through a viscous barrier[5,9] is another crucial property, and it is mandatory to achieve the best postoperative outcomes.[1,14–16]

After the development of the first OVD agent composed of a sodium hyaluronate 1.0% solution (Healon), additional types of OVDs were developed including various mixtures of sodium hyaluronate and chondroitin sulfate. Other materials, such as hydroxypropyl methylcellulose, were also used to produce OVDs. At present, many OVDs are commercially available. Ophthalmic viscosurgical devices have been initially classified as high-viscosity cohesive agents and low-viscosity dispersive agents.[17] The introduction of sodium hyaluronate 2.3% solution (Healon5) in 1998 added a new category of OVDs termed viscoadaptive.[18]

The viscous cohesive devices stay together as 1 unit during surgery. On the other hand, the dispersive agents have an intermolecular structure weak enough to break apart, even when exposed to low stress at low shear rates. The rheological behavior of viscoadaptive OVDs changes under different stress conditions; a superviscous, very cohesive behavior prevails at low-frequency stress, while the OVDs become almost solid and literally fracture when exposed to high-frequency stress.[19]

The ability to maintain space maintenance is related to the zero shear rate viscosity of OVDs, which determines

Submitted: June 29, 2016 | Final revision submitted: November 4, 2016 | Accepted: November 4, 2016

From the Eye Clinic (Tognetto, D'Aloisio, Cecchini) and the Department of Engineering and Architecture (Lapasin), University of Trieste, Trieste, Italy.

Corresponding author: Paolo Cecchini, MD, PhD, Istituto di Clinica Oculistica, Università di Trieste, Ospedale Maggiore, Piazza Ospedale, 134129 Trieste, Italy. E-mail: paolo.cecchini@ymail.com.

Published by Elsevier Inc.

0886-3350/$ - see frontmatter
http://dx.doi.org/10.1016/j.jcrs.2016.11.035

the flow properties of the fluid at very-low-frequency stress and velocity gradients. For polymer solutions, such rheological characteristics are directly proportional to their polymer molecular weight and concentration. The same applies for hyaluronan solutions, which are the most widespread OVDs, and attain high viscosity values at high polymer concentrations, high molecular weights, or both.

In contrast, dispersion the main property that protects the endothelial cells.[1,20,21] An OVD is required to shield the endothelium during surgery. The ability to coat tissue and to be retained during surgery is inversely related to the molecular weight and the surface tension. Therefore, dispersive OVDs have a low molecular weight and a low surface tension.

The average molecular weights and the concentrations of sodium hyaluronate polymers vary for different commercially available OVDs, yielding products with different viscosities at different shear rates. The rheological characteristics of the OVDs directly affect their clinical performances.[5,9]

In the present study, we assessed the rheological properties of different OVDs. Formulations comprising a mixture of 2 OVDs with different molecular weights and concentrations were analyzed to evaluate a new category of OVD resulting from combining molecular chains of different length. A new viscous dispersive OVD was evaluated for comparison.

MATERIALS AND METHODS

Blends of 2 OVDs were prepared using a super viscous cohesive agent (Healon GV, Abbott Laboratories, Inc.) comprising sodium hyaluronate solution 1.4% and a medium-viscosity dispersive OVD (Viscoat, Alcon Laboratories, Inc.) comprising sodium hyaluronate 3.0%–chondroitin sulfate 4.0%. Specifically, a formulation made up of 1 part of the superviscous cohesive OVD and 1 part of the medium-viscosity dispersive OVD and a formulation made up of 3 parts of the superviscous cohesive OVD and 1 part of the medium-viscosity dispersive OVD were tested. A viscous dispersive OVD, containing sodium chondroitin sulfate 4.0% and sodium hyaluronate 1.65% in solution (Discovisc, Alcon laboratories, Inc.) was tested in comparison (Table 1).

The OVD blends were prepared by pouring appropriate amounts of the 2 components into a small glass petri dish in the selected proportions and then mixing them with a magnetic stirrer for 15 minutes to ensure adequate blend homogeneity. Samples were stored at a constant temperature of +4°C, and rheological analysis was performed at 25.0°C ± 0.1°C (SD) with a controlled stress rheometer (Haake RS-150, Haake GmbH) equipped with a parallel-plate measuring device (PP 35 Ti, Haake GmbH) with serrated surfaces, a diameter of 35.0 mm, and a gap of 1.0 mm. The oscillatory rheometer gives a measure of the viscosity known as complex viscosity (η^*), which is calculated from the elastic modulus, the viscous modulus, and the frequency of the oscillation.

The steady flow behavior of the samples was determined using the same geometry as for the oscillatory tests and applying a stepwise procedure composed of constant stress segments. Thus, the zero shear rate viscosity (η_0) for each formulation was derived from the flow curves and obtained from the shear thinning η versus σ profile, using the Cross model for data fitting.

Small amplitude oscillatory tests were performed for each OVD sample at a constant strain (1.0%) to characterize the linear viscoelastic properties over a range of frequencies (0.01 to 100.00 Hz). Stress sweep procedures were previously performed to evaluate the upper limit of the linear viscoelastic regimen and hence to select the strain condition of the frequency sweep tests. Linear conditions mean that the strain (the amount by which the sample is deformed) is linearly proportional to the applied stress the force per unit area (Pa) required to deform the sample. Measurements of linear viscoelasticity ensure a relatively simple treatment and more significant interpretation of the experimental results.[22]

The profiles of the storage modulus G' (elasticity) and the loss modulus G'' (viscosity) obtained from frequency sweep tests are similar, resembling those of concentrated polymer solutions. Thus, the crossover condition (ω_{cr}, G_{cr}) can be individuated for all the systems.

The stress sweep procedures were previously applied to evaluate the upper limit of the linear viscoelastic regimen and, hence, select the strain condition of the frequency sweep tests. Pseudoplasticity was evaluated for each OVD studied. The experiments were performed in duplicate on each sample to confirm the reproducibility of the results.

RESULTS

Figure 1 shows the frequency responses of the OVDs. The storage modulus (G'), the loss modulus (G''), and the crossover points are plotted against the oscillatory frequency ω. The crossover point of the superviscous cohesive OVD occurs

Table 1. Sodium hyaluronate and chondroitin sulfate molecular weight and concentration of the OVDs analyzed.

	Characteristic				
OVD	NaHa (%)	NaHa MW	CDS (%)	CDS MW (K)	CDI
1 Healon GV	1.40	5.0 M	—	—	72
2 Viscoat	3.00	500 K	4	25K	3.5
3 Discovisc	1.65	1.65 M	4	25K	12
4 Healon GV:Viscoat 1:1					
Healon GV	0.70	5.0 M	—	—	—
Viscoat	1.50	500 K	2	25K	—
4 Healon GV:Viscoat 3:1					
Healon GV	1.05	5.0 M	—	—	—
Viscoat	0.75	500 K	1	25K	—

CDI = cohesion–dispersion index; CDS = chondroitin sulfate; MW = molecular weight; NaHa = sodium hyaluronate