From Simple Liquids to Surgical Instruments: On the History of Ophthalmic-Viscosurgical Devices (OVD)

Summary
Nowadays, OVDs are regarded as standard tools in ophthalmic surgery. Their discovery and development started about 70 years ago, in 1934, with isolating hyaluronic acid as the substance of the vitreous body of the human eye. Sodium Hyaluronate was the first substance used as an OVD and is now the most widely used material for OVDs used in ophthalmic surgery. It has become "the gold standard" to which all other viscoelastics are compared. Since the introduction of viscoelastic substances in the 1970s the properties of these agents have improved the quality of anterior segment surgery. Therefore OVDs had — and still have — a great impact on the success of ophthalmic surgery — especially of cataract surgery and intraocular lens implantation. In vivo studies have proven that the molecular and chemical structure of hyaluronic acid is ideal. Interactions between molecules and receptor tissues and inflammatory and immunogenic reactions have also been studied extensively. This article shows the historical development of the different substances used nowadays and their properties.

Keywords: history, Ophthalmo-Viscosurgical Devices, OVD, viscoelastic substances, hyaluronic acid

Streszczenie

Słowa kluczowe: historia, preparaty wiskoelastyczne, OVD, substancje wiskoelastyczne, kwas hialuronowy
Introduction
Nowadays, Ophthalmic viscosurgical devices (OVD) are regarded as standard tools in ophthalmic surgery. Their discovery and development started approximately 70 years ago, in 1934, with isolating hyaluronic acid as the substance of the vitreous body of the human eye. This article shows the historical development of today’s different used substances and their properties. Today, hyaluronic acid is more and more used in eye drops and contact lens rewetters due to its high wetting and water binding properties. Therefore, this article will review the historical development and usage of this compound in cataract surgery.

Material and Methods
The outcome of this article is based on an intensive research of current and historic literature on the topic in discussion. This article evaluates 65 scientific articles on the topics hyaluronic acid and ophthalmic viscosurgical devices.

Results
OVDs (Ophthalmic Visco-surgical Devices) [1] — formerly called viscoelastics or viscoelastic substances — are a class of non-active clear gel-like chemical compounds with viscous and elastic properties [2]. The specific physical properties make them useful e.g. for ophthalmic surgery, mainly cataract surgery [3]. (Here) they create and maintain the anterior chamber depth and visibility, protect the corneal endothelium and other intraocular tissues during surgery. OVDs minimize interaction between tissues and instruments during surgery and ensure therefore high tissue integrity [4, 5].

OVDs are essential in ophthalmic surgery today. Their use became increasingly popular for cataract surgery, glaucoma surgery, cornea surgery, trauma surgery, and vitreoretinal surgery [6, 7].

Since the introduction of viscoelastic substances in the 1970s the properties of these agents have improved the quality of anterior segment surgery.

OVDs are clear viscous fluids used in ophthalmic surgery, packed in a syringe, and are delivered through a cannula into the eye. Based on their properties, OVDs can be divided into two groups [8]:

— Cohesive agents show high viscosity, adhere to themselves, and act like a gel. The molecules are long chains, have a high molecular weight, and show high pseudoplasticity and surface tension.

— Dispersive agents show low viscosity, the molecules behave separately, they build up a solution. They show low pseudoplasticity and surface tension with short chains and low molecular weight.

Historical background
In 1934, Meyer and Palmer were able to isolate hyaluronic acid, a polysaccharide from the vitreous cortex [9, 10]. Hyaluronic acid was also purified from umbilical cord and rooster combs by Endre Balazs [11]. In 1958, he has been the first who suggested the use of hyaluronic acid as a possible vitreous substitute in the performance of complicated retinal detachment surgery [12]. In 1972, Balazs performed the first intravitreous injection of hyaluronic acid [13].

Miller and Stegman suggested the use of hyaluronic acid during the implantation of intraocular lenses [14]. Sodium hyaluronate was used in 1977 by Miller to perform experimental IOL (Intra-Ocular Lens) implantation in rabbit eyes [15]. In the same year, Fechner used a 1% solution of methylcellulose to maintain the volume of the anterior chamber [16]. Beside of Fechner different other surgeons described methylcellulose as an inexpensive alternative to hyaluronic acid used as an OVD [17, 18].

In 1979, during a symposium on oculomotor surgery, Balazs presented the patent of viscoelastic material with high molecular weight ("HMW VE NIF-NAHA") [19] consisting of purified hyaluronic acid, which was used in an IOL implantation procedure. At the same video symposium, a new terminology "Viscosurgery" was born, also coined by Balazs. In the same year Balazs sold his US-patent to the company Pharmacia which developed the first viscoelastic product (Healon®), also in 1979. Healon* is today still available distributed by AMO (Abbott Medical Optics).


Since the introduction of Healon® (sodium hyaluronate, 1%), ophthalmic viscosurgical devices have become essential tools, particularly in anterior segment surgery. The use of OVDs creates and maintains anterior chamber depth and visibility. It protects the sensitive endothelium and other intraocular tissues, and minimizes interaction between tissues and instruments during surgery [20–22]. Space and surface tactical aspects of OVD...
application have first been shown by Eisner [23], techniques like visco-blockade, — tamponade or — spatula have been invented by him [24].

Therefore OVDs had — and still have — a great impact on the success of cataract surgery and intraocular lens implantation [25-30].

From 1995 to 2000 ISO developed an International Standard for the safety, performance and approval requirements for viscoelastics under a new designation of Ophthalmic Viscosurgical Devices (OVDs) [31].

Additionally, the development of new surgical techniques in cataract extraction procedures such as phacoemulsification, invented by Charles Kelman 1967, and foldable IOL implantation (since 1988) was accompanied by the development of new modalities of viscoelastics.

Viscoelastics have a wide range of features with rheologic-related properties such as viscosity, elasticity, pseudo-plasticity, cohesiveness, etc. [32-34]. Although the properties exist independently, they act synergistically. The same viscoelastic can be used as a different tool according to specific needs, such as separating or joining tissues, maintaining space, or protecting surfaces (i.e. corneal endothelium, lens capsule or anterior hyaloid) from mechanical trauma or fluids infusion.

Viscosurgery procedures are not limited to cataract surgery. They are now routinely used in anti-glaucoma filtering surgery, combined surgical interventions, keratoplasty, and anterior vitrectomy [35, 36].

In corneal surgery, Alpar observed reduced endothelial cell loss in various keratoplasty procedures performed with Healon® in 1984 [37]. Findings of reduced complication rate with OVDs have been confirmed by other studies. Beside protection, an OVD depot (dome) supports and stabilizes the donor cornea (cushion) after removal of recipient cornea, and facilitates positioning. Healon® 5, a new, high concentration viscoadaptive OVD becomes more and more popular for this procedure.

In glaucoma surgery, anterior chamber collapse during trabeculectomy is a common complication and plays an important role in cataract formation following glaucoma surgery. Also, less post-op hyphemata is observed. OVDs in other glaucoma procedures are used to improve visibility, avoid bleeding (tamponade), or open chamber angles.

In trauma surgery OVDs are used in treating perforating bulbar injuries (stabilizing anterior chamber, separating of tissue). They provide a better overview at operation site by improving the visibility of the injured anatomic structure. Furthermore, OVDs reduce intraocular bleeding, and foreign bodies can be moved/removed very safely.

The usage of OVDs in vitreoretinal surgery is related to the early history of OVDs. With new agents for the use in the posterior segment — like gases, perfluorocarbons, or silicone oil — as endotamponade, the importance of OVDs have decreased.

Substances used as ophthalmo-viscosurgical devices

Sodium Hyaluronate was the first substance used as an OVD and is now the most widely used material for OVDs used in ophthalmic surgery. It has become “the gold standard” to which all other viscoelastics are compared [38].

Hyaluronic acid (Sodium Hyaluronate, NaHa) [39-45] is a linear polysaccharide molecule of sodium glycuronate and N-acetyl glucosamine. The molecular weight may range from 100,000 to 7 million Daltons; the molecule consists of nearly 10,000 disaccharide units. Hyaluronic acid which is used in OVDs is primarily extracted from rooster combs. It is a natural biological substance in all vertebrates, humans, and also some bacteria. High concentrations are found in human connective tissue and in the eye (vitreous, cortex, and trabecular meshwork), low concentrations in aqueous humor and corneal endothelium. Hyaluronic acid seems to be recently the most widely used OVD worldwide.

![Fig. 1. Chemical structure of hyaluronic acid](image1.png)

Chondroitin Sulfate (CS) [46], [36] is like hyaluronic acid a biological substance in the extracellular matrix mainly in solid tissue parts like cartilage or corneal stroma. For use the as an OVD the polysaccharide is mainly extracted from shark-fin cartilage. Molecular weight is about 20,000 D, the chain length 50 nm which gives the molecule a lower viscosity and negative charge.

![Fig. 2. Chemical structure of Chondroitin sulfate](image2.png)
Methylcellulose (MC) \([47-49]\) is widely distributed in cotton and wood but not in humans or animals. It is a disaccharide (glucose units) with side chains to make the molecule more hydrophilic. In ophthalmology methylcellulose is used as a lubricant because of its good wetting and coating capacity. From an immunological aspect it is important that this substance does not occur naturally in the human body, and therefore shows a significant inflammatory potential. It will not be metabolized completely.

Polyacrylamide is a synthetic polymer with a high molecular weight derived from acrylamide which consists of long carbon chains. The product was withdrawn from the market in 1991 after observing intraocular pressure elevation treated with this material. Poyacrylamid is today only of historical interest \([7]\).

Collagen as a viscoelastic material consisting of Type IV collagen can be extracted from human tissue as well as from animal tissue (pigs). Up to now, there is less information about the ideal origin of this substance for using it as OVD \([7]\).

Further substances as a basis for OVD were suggested but attained however no clinical relevance \([50]\).

**Rheological and physico-chemical properties of substances used as ophthalmo-viscoelastic devices**

The description and characterization of different viscoelastic substances is a prerequisite for understanding their specific properties and from this their intended use. A profile of requirements for daily surgical practice can be established which indirectly presupposes the existence of certain physico-chemical characteristics. These substances must be easily and quickly injected, protect the corneal endothelium, and have the capacity to create and maintain intraocular space or compartments. It is important that optimal sight, i.e. optimal transparency of the material, is established during surgery. During the last stage of surgery the substance should be both, easily and quickly removable, or be naturally digested in the eye. In either case there should be no rise in intraocular pressure during the early postoperative phase.

Some of these functions are contradictory: Water-based solutions are most easily injectable since they offer almost no resistance. Viscous or viscoelastic substances are slower to flow through a cannula; moreover this speed is dependent on cannula diameter and pressure on the plunger.

Additionally, corneal endothelial protection presupposes a certain stickiness and adhesion of the viscous substance to the tissue, which makes the removal of the substance more difficult. A strong space-maintaining capacity can also cause problems during the removal of the substance. The characteristics mentioned before can be described by the properties of the specific visco-surgical device, like: viscosity, elasticity, viscoelasticity, pseudoplasticity, cohesion, and its contact angle.

Viscosity is a measure of fluidity resistance of a fluid, indicating how viscous a substance is. Viscosity is dependent on several factors including molecular weight, molecule size, concentration, and temperature. Viscosity can be measured physically by placing the substance between two parallel plates and then moving these against each other. The “frictional resistance” of a viscoelastic can thereby be quantified. During this experiment the following terms are also interesting for day to day clinical use. The shear rate represents the speed with which the plates are shifted against each other (Unit rad/s = radiant per second or hertz = Hz, 1/second). The force needed to shift the plates per surface unit is called shear force (unit dynes/cm²). The so-called velocity gradient refers to the ratio between the relative speed of shifting the disk and thickness of the substance between the disks. This term is important since the quotient of shear force and velocity gradient is the measure of dynamic viscosity (unit N x sec x m⁻² = Poise, P for Poiseille). The quotient of dynamic viscosity and fluid density is called kinematic viscosity (unit Stokes, St).

Zero Shear Viscosity refers to viscosity at rest, i.e. at a shear rate of zero. This term is frequently seen as particularly characteristic of viscoelastics. It is interesting to note that there is practically no way in which this value can be measured and is therefore always theoretically calculated through extrapolating. This value should be surveyed censoriously and not used as an exclusive measure to judge a viscoelastic. A practical value of this measure exists nonetheless, for example good space-maintaining capacity can be achieved with a high zero shear viscosity, meaning that a deepening of the anterior chamber and the creation of space is highly successful. Comparatively, a viscoelastic with low zero shear viscosity, as in cases of high vitreous pressure can flow out of the incision.

The next term to be considered is of the term elasticity. In the physical sense, elasticity describes the ability to...
offer resistance to a force and the ability of a substance to return to its original form following the removal of the force. Elasticity is also dependent on molecular weight and concentration, and is influenced by the frequency of the influencing force as well. Hyaluronic acid preparations tend to behave like viscous fluids in a low frequency range (0.1 to 10 Hertz) and more like elastic bodies at higher frequencies.

The term viscoelastic gives a name to an entire substance group. It is a term that describes substances which can behave both, viscous and elastic. Viscoelastic substances offer low resistance towards deforming forces and do not have the ability to immediately return to their original form, and indeed will never be able to fully reach their original form. This refers to relative form stability.

As a rule, all viscoelastics consist of a molecular network with varying concentrations. Most viscoelastics behave viscous if a force with low speed and low frequency act on them. The added energy is converted to heat, since the molecular chains shift against each other. At higher frequencies or fast energy impact, the viscoelastic acts like a shock absorbing gel cushion. Elastic energy is elastically stored and dispensed with relative form stability. Which of the characteristic above prevails is dependent upon the type of force effect, and in particular the concentration and temperature. The above described characteristic of viscoelasticity is also referred to as pseudoelasticity.

Natrium hyaluronates show the highest pseudoelasticity. For practical purposes this means that they have high viscosity (zero shear viscosity) at rest. Therefore, they have good space-maintaining capabilities. Less viscous chondroitinsulfate-natrium hyaluronate combinations such as Viscoat (Alcon) have better coating capabilities. Low pseudoelasticity of chondroitinsulfate leads to the substance adhering longer to the corneal endothelium and therefore not being rinsed out of the eye as quickly as hyaluronic acid preparations which have the tendency to quickly rinse out of the eye “en bloc”. This is a particular advantage during phacoemulsification where relatively high volumes of fluid are used.

A further term that describes the properties of viscoelastics is coating ability. This refers to the degree of adhesion of a viscoelastic on a surface. It is ascertained through the contact angle of the substance with the surface and surface tension. When a substance forms a strong curvature change on the surface, a large contact angle is formed. This points to little adhesion. For clarification, an extreme case of this would be a drop of water that repels off the surface of a Gore-Tex jacket.

Two further terms that are often associated with the characterization of viscoelastics are cohesion and dispersion. Cohesion refers to extent to which a viscoelastic substance is held together through intermolecular bindings and molecular chains. Higher molecular viscoelastics (e.g. Healon GV (AMO)) with long molecular chains are cohesive. A substance like this can escape or be rinsed out of the eyes “en bloc” during aspiration. Dispersive viscoelastics (e.g. Viscoat (Alcon)) are generally low molecular with shorter and less tightly weaved molecular chains. They do not leave the eyes “en bloc” but rather show a tendency to become glued to the structures and are therefore often difficult to aspirate. A description of cohesion and dispersion of different viscoelastics was put forth in an experimental study through means of the Cohesion-Dispersion-Index (CDI) [70]. The CDI represents the quotient of the share of the aspirated viscoelastic in percentage, measured in time and the respective aspiration setting. The faster and the more viscoelastic could (or can??) be removed, the higher the CDI. This would be e.g. 72,3 for Healon GV (AMO), 46 for Provisc (Alcon), 21,4 for Healon (AMO) and 3,4 for Viscoat (Alcon).

Most important is still the use of viscosurgical devices in cataract surgery. During the manipulation of capsulorhexis it is also important that the anterior chamber remains stable, once again making high viscosity important. While good pseudoplasticity is most important in nucleus expression, low cohesion and high dispersion are essential during phacoemulsification, preventing the viscoelastic from being rinsed out of the eye. This also applies to the steps of irrigation/aspiration during cortical cleanups. Opening and stabilizing the capsular bag for IOL-implantation requires a good space-maintaining capacity and therefore high viscosity and pseudoplasticity. Good cohesion, meanwhile, is helpful for a fast and complete removal of the substance [1, 4, 6, 7, 10, 34–36].

**Viscoelastic devices used in ophthalmology**

The physico-chemical properties of viscoelastics described above allow them to be used in a variety of ways and carry out a number of different functions. Particularly in cataract surgery there is a demand for the “ideal” viscoelastic which requires partly contradictory characteristics. For clinical purposes it is therefore an advantage to have in-depth knowledge of the individual properties in order to use specific substances or a combination of substances depending on the circumstances.

An integral function of viscoelastics is to maintain the anterior chamber not only during cataract surgery, but also during other corneal surgical procedures, glaucoma surgeries, trauma, and revision-surgeries in the anterior eye segment. The viscosity and elasticity of a substance determine of how well the viscoelastic is fulfilling its intended task. HPMC-preparations show little elastic-
ility; therefore they are leaving the eye relatively quickly through the incision in cases of elevated vitreous pressure. Sodium hyaluronate products, in particularly those of higher concentrations, can maintain anterior chamber depth due to their high elasticity.

A further function is the mobilization and forcing back of tissues in the anterior chamber. Examples of this in cataract surgery are the gentle loosening of synechiae between iris and lens, viscomydriasis for pupillary dilation, and filling the lens capsule prior to implantation.

Viscoelastics can perform a protective function through the coating of instruments, implants and tissue surfaces (e.g. corneal endothelium). Prerequisites for this are low surface tension and a small water contact angle. HPMC-preparations as well as the combination preparation Viscoat® (Alcon) containing chondroitin sulfate and sodium hyaluronate, possess significantly lower surface tension and water contact angles than pure sodium hyaluronate preparations, particularly those with high concentration and high molecular weight. Liquids spread more easily when their surface tension is lower than the critical surface tension of the tissue [65]. The critical surface tension of the corneal endothelium lies between 43 and 63 dyne/cm. The surface tension for HPMC-preparations should be at 43.0±1.41 dyne/cm, and at 62.7±6.51 dyne/cm for Healon [64]. Details concerning the contact angle for various preparations are provided in table 3.1.1. For this, the contact angle was measured at 3° Celsius under nitrogen on PMMA [65].

Coating the corneal epithelial surface with viscoelastic, leads to a thorough, long-lasting moistening of the cornea with corresponding positive effects on the clarity of the cornea. In addition, a drop of viscoelastic can act like a magnifying lens and therefore further improve the view in the anterior chamber. The protection of the corneal endothelium represents an important function of a viscoelastic. In contrast to the corneal epithelium, the single-layered endothelium is not capable of regeneration following damage. Various factors can lead to the damage of the endothelium during intraocular surgery. The endothelium can come in direct contact with lens fragments, instruments or the IOL. Furthermore the turbulence of the irrigation fluid can affect the endothelium. Air bubbles, free radicals, and sound waves developed during phacoemulsification can also damage endothelial cells. The space-maintaining function of viscoelastics indirectly contributes to endothelial protection because the space for intraocular manipulation is maintained. Coating of the endothelium, instruments and the IOL represent a further protective factor. Specific sodium hyaluronate binding areas were proven to be present at the endothelium [66–68]. It is assumed that sodium hyaluronate containing products are able to offer a special protective function because of this. The continuous coating of the endothelium, in particular offered by dispersive low-viscous substances, is generally seen as an important protective factor. An overly extensive removal of the viscoelastic with the corresponding irrigation/ aspiration in the endothelial area may lead to endothelial damage, hence when using preparations such as Viscoat (Alcon), a thin layer can remain on the cornea.

Beside cataract surgery, viscoelastic devices are also used in other fields of ophthalmology, e.g. in kerato-plasty- and glaucoma-, vitreoretinal-, and trauma surgery. Because of its extreme high ability to bind water relative to its mass this substance is therefore also used in numerous formulations of eye drops used for dry eye symptoms [10, 33–37, 45, 46].

Complications using viscoelastic substances in ophthalmology

The use of viscoelastics can also lead to intraoperative and postoperative complications. Intraocular structures can be damaged by overfilling the eye (zonular or capsular rupture) or by incomplete removal at the end of surgery (postoperative increase of intraocular pressure). An overfilling of the eye depends more on the experience of the surgeon than on the type of viscoelastic. However, viscoelastics behave very individually during the removal process. Viscoelastic that is left in the eye generally escapes as a large molecule by means of the trabecular meshwork. The ability of the viscoelastic to drain through this manner can be influenced by a variety of factors.

Hyaluronic acid used as viscoelastic substance in other areas in medicine

Hyaluronic acid is an important structure-forming matrix in the human body, particularly in the joints. There hyaluronic acid is responsible for the strength (viscosity) of joint fluid (synovial fluid) and thus also crucial for the nutrition of the cartilage. Like a film, hyaluronic acid covers the cartilage, smoothes and lubricates the surface. In osteoarthritic patients the synovial fluid shows a lower content of hyaluronic acid as in healthy patients. By this viscosity and elasticity of the synovial fluid is greatly altered. Hyaluronic acid injections replace or complement the mutated synovial fluid in osteoarthritis. These injections may stimulate the administration of hyaluronic acid in the joints and the cells of the synovium to the increased production of endogenous hyaluronic acid. Therefore hyaluronic acid is also widely used in human orthopedics as well as in veterinary medicine. Hyaluronic acid reduces the symptoms of most patients. An improvement of already existing alterations
Mayor ophtalmo-movicosirgical products used in ophthalmology today

At present a multitude of different viscoelastics are available on the market. Most products contain sodium hyaluronate in different concentration followed by different HPMC preparations.

Viscoelastics can be classified according to their viscosity, cohesiveness and dispersiveness; it can be distinguished between the following groups [1, 36]:

High viscous-cohesive viscoelastics:
- Molecular weight 5,000,000 to 7,900,000 Dalton,
- Zero shear viscosity: > 1,000,000 mPs

(Examples: Healon GV (AMO), Healon 5 (AMO))

Viscous-cohesive viscoelastics:
- Molecular weight 100,000 to 6,100,000 Dalton,
- Zero shear viscosity: < 100,000 mPs to 100,000 mPs

(Examples: Healon (AMO), Provisc (Alcon),
Allervisc (Allergan), Amvisc (Bauch + Lomb))

Middle viscous-dispersive viscoelastics:

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**TAB. 1. Selection of sodium hyaluronate based viscoelastics**

<table>
<thead>
<tr>
<th>PREPARATION</th>
<th>POLYMER</th>
<th>CONCENTRATION</th>
<th>MANUFACTURER/DISTRIBUTOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healon</td>
<td>Sodium hyaluronate</td>
<td>1.0%</td>
<td>AMO</td>
</tr>
<tr>
<td>Healon 5</td>
<td>Sodium hyaluronate</td>
<td>2.3%</td>
<td>AMO</td>
</tr>
<tr>
<td>Healon GV</td>
<td>Sodium hyaluronate</td>
<td>1.4%</td>
<td>AMO</td>
</tr>
<tr>
<td>Vitrax II</td>
<td>Sodium hyaluronate</td>
<td>3.0%</td>
<td>AMO</td>
</tr>
<tr>
<td>Amvisc</td>
<td>Sodium hyaluronate</td>
<td>1.0%</td>
<td>B&amp;L</td>
</tr>
<tr>
<td>Amvisc Plus</td>
<td>Sodium hyaluronate</td>
<td>1.6%</td>
<td>B&amp;L</td>
</tr>
<tr>
<td>Provisc</td>
<td>Sodium hyaluronate</td>
<td>1.0%</td>
<td>Alcon</td>
</tr>
<tr>
<td>Viscoat</td>
<td>Sodium hyaluronate Chondroitinsulfate</td>
<td>3.0%</td>
<td>Alcon</td>
</tr>
<tr>
<td>DuoVisc</td>
<td>Sodium hyaluronate Chondroitinsulfate</td>
<td>See Viscoat and Provisc</td>
<td>Alcon</td>
</tr>
<tr>
<td>DisCoVisc</td>
<td>Sodium hyaluronate Chondroitinsulfate (combination package of Viscoat and Provisc)</td>
<td>1.7%</td>
<td>Alcon</td>
</tr>
<tr>
<td>Visthesia 1.0 and 1.5</td>
<td>Sodium hyaluronate lidocaine (1.0)</td>
<td>1.0%</td>
<td>Zeiss</td>
</tr>
<tr>
<td>Rayvisc</td>
<td>Sodium hyaluronate</td>
<td>3.0%</td>
<td>Rayner</td>
</tr>
</tbody>
</table>

**TAB. 2. Selection of different HPMC products**

<table>
<thead>
<tr>
<th>PREPARATION</th>
<th>POLYMER</th>
<th>CONCENTRATION</th>
<th>MANUFACTURER/DISTRIBUTOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adatocel</td>
<td>HPMC</td>
<td>2.0%</td>
<td>B&amp;L</td>
</tr>
<tr>
<td>Coatel</td>
<td>HPMC</td>
<td>2.0%</td>
<td>B&amp;L</td>
</tr>
<tr>
<td>HPMC-Ophthal H</td>
<td>HPMC</td>
<td>2.0%</td>
<td>Dr. Winzer</td>
</tr>
<tr>
<td>HPMC-Ophthal L</td>
<td>HPMC</td>
<td>2.0%</td>
<td>Dr. Winzer</td>
</tr>
<tr>
<td>La Gel</td>
<td>HPMC</td>
<td>1.8%</td>
<td>LA Labs</td>
</tr>
<tr>
<td>Ocucoat</td>
<td>HPMC</td>
<td>2.0%</td>
<td>B&amp;L</td>
</tr>
<tr>
<td>Visco Shield 2%</td>
<td>HPMC</td>
<td>2.0%</td>
<td>Domilens</td>
</tr>
</tbody>
</table>
Medicals Int. have been studied extensively.

**Discussion**

Development, production and use of OVD require ongoing research to evaluate the biocompatibility, purity, and ocular structure protection of the materials in question [51-63]. In-vivo studies have proven that the molecular and chemical structure of hyaluronic acid is ideal, and interactions between molecules, receptor tissues [64], inflammatory and immunogenic reactions [65] have also been studied extensively.

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**References**

9. Meyer K., Palmer J.W., — Zero shear viscosity: <100,000 mPs> 10,000 mPs (Examples: Viscoat (Alcon), Cellugel (Alcon))
10. Balazs E.A., Freeman M.I., Kloti R., et al., — Molecular weight 86,000 to 90,000 Dalton, — Zero shear viscosity: <10,000 mPs > 1,000 mPs (Examples: OcuCoat (Bauch + Lomb), Adatocel (Bausch + Lomb))

As far as the authors can evaluate, mayor ophthalmic-viscosurgical products on the European market are the following in regards of their ingredient(s) (table 1 and 2).


69. Bausch + Lomb, Berlin (D), product information on Bloxaphte available [online], http://www.bloxaphte.de.