New generation hydroxypropyl methylcellulose (HPMC-Ophtal H) for intraocular surgery: a confocal laser scanning microscopy study

N. RAY-CHAUDHURI,
D.G.R. JAYAMANNE, N.P. STRONG

LABORATORY STUDY

Abstract

Purpose **To determine the abundance and variety of particulate debris in new generation hydroxypropyl methylcellulose (HPMC) samples.**
Method **Three samples of sterile HPMC-Ophtal H were examined using a confocal laser scanning microscope, scanning electron microscope and mass spectrometry.**
Results **Confocal laser scanning microscopy of the samples showed that particulate matter in HPMC was less than 30 μm in size and at a density of less than 1000 particles per millilitre. No discernible details were seen by the scanning electron microscope, and mass spectrometry did not identify any bands.**
Conclusion **Improved methods of preparation including filtration may be responsible for decreased particulate debris in new generation HPMC.**

Key words Cataract surgery, Confocal laser scanning microscope, Viscoelastics

Methylcellulose has been used since the mid-1970s to prevent damage to endo-ocular tissue, especially endothelial cells, during surgery.[1] Many studies have demonstrated that hydroxypropyl methylcellulose (HPMC) appears to be non-inflammatory and tolerated by the eye.[2–4] Studies comparing HPMC and sodium hyaluronate in extracapsular cataract surgery have shown that both agents helped to maintain the anterior chamber equally well and no statistically significant difference was noted in immediate post-operative intraocular pressure and long-term endothelial cell loss between the two groups.[3,5,6] A study investigating the rate and ease of removal of viscoelastic materials following cataract surgery concluded that most of the HPMC used for the procedures can be aspirated using an automated irrigation/aspiration device within 1 min.[7] However, the use of HPMC as a viscoelastic solution for intraocular surgery decreased in popularity in the late 1980s due to concerns about possible adverse effects of particulate debris of botanical origin found in samples of HPMC from United Kingdom hospital pharmacies.[8]

Phacoemulsification allows a smaller wound combined with a tunnel that has a degree of self-sealing. A positive intraocular pressure is easier to maintain with this type of wound. New generation HPMC has been advanced as a satisfactory viscoelastic in small-incision cataract surgery, thereby offering a cost-saving on these procedures.

We studied the new generation pre-packed single-use samples of HPMC for debris of botanical nature using the confocal laser scanning microscope, which is an extremely powerful research tool used to visualise both living and fixed material. Particles of cellulose origin demonstrate autofluorescence under the 488 nm laser line.

Methods and results

Three samples of sterile HPMC-Ophtal H were examined. This commercially available viscoelastic material, manufactured by LCA SA, France and distributed by Vision.Net.UK, has the following composition: methylhydroxypropylcellulose (20 mg/ml), sodium chloride (9 mg/ml), boric acid (2.7 mg/ml), borax (0.2 mg/ml) and water. In addition to using the confocal laser scanning microscope (CLSM), scanning electron microscopy (SEM) and mass spectrometry were used to demonstrate whether significant particulate debris was present.

N. Ray-Chaudhuri
D.G.R. Jayamanne
N.P. Strong
Department of Ophthalmology
Royal Victoria Infirmary
Newcastle upon Tyne, UK

Mrs N. Ray-Chaudhuri ✉
Department of Ophthalmology
Royal Victoria Infirmary
Newcastle upon Tyne
NE1 4LP, UK

Tel: +44 (0)191 227 5065
Fax: +44 (0)191 227 5246

The authors have no proprietary interest in HPMC-Ophtal H

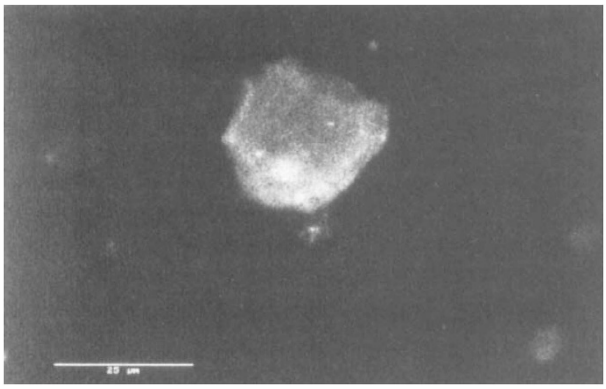

Fig. 1. *The confocal laser scanning microscope image showing a particle of cellulose origin demonstrating autofluorescence.*

Confocal laser scanning microscopy

A drop of the samples was placed on a pre-cleaned microscope slide and covered with a cleaned coverslip. The mount was ringed with clear nail varnish to prevent evaporation and allow examination with the oil immersion lens. Using a MRC 600 CLSM equipped with a krypton/argon laser the specimen was scanned with the 488 and 568 nm wavelength lines, using the ×40 numerical aperture 0.7 lens. Particulate debris of botanical origin should demonstrate autofluorescence under the 488 nm laser line. A small amount of autofluorescence was noted (Fig. 1). An image was acquired from the 488 nm channel which was a reconstruction of a six-step Z series (images from cuts of 12 μm depth through the specimen). This image was thought to show a few particles of cellulose origin no greater than 30 μm in size. The image was stored on an optical disc and printed out on a Sony up-890CE thermal printer.

Scanning electron microscopy

A drop of the samples was placed on a cleaned glass coverslip and then coated with 10 μm of gold. Under SEM the sample showed no discernible details.

Mass spectrometry

Samples were analysed using a mass spectrometer. These were first spun, and the fractions compared. No bands were identified, inferring no large particles were present.

Discussion

Previous examination of HPMC samples prepared for intraocular procedures showed that the material contained a variety of particulate debris of botanical origin ranging from 20 to 100 μm in size at a density of between 1000 and 800 000 particles per millilitre.[8] This study concluded that methods of preparation of HPMC by United Kingdom hospital pharmacies were at best ineffective in purifying the material.[8]

We studied the new generation of HPMC samples using the CLSM. This is an extremely powerful research tool that allows investigators to visualise both fixed and living material with far greater clarity than is obtainable using standard microscopy techniques. The microscope works by using a highly focused laser beam to systematically scan across the specimen and then selectively detect the light given off from the small volume of tissue illuminated. The laser can scan up and down through the specimen, thus obtaining a series of optical sections.

Due to particles of cellulose origin demonstrating autofluorescence under the 488 nm laser line it was possible to obtain an accurate objective assessment of the HPMC samples. Our observations confirmed that the HPMC was of cellulose origin. However, the particulate matter was less than 35 μm in size and the abundance was far less than 1000 particles per millilitre. We conclude that probable improved methods of preparation including filtration may account for the observed difference in particulate matter in the new generation HPMC samples. The CLSM observations were confirmed by mass spectrometry, which failed to demonstrate bands, inferring no large particles were present in the studied material.

New generation HPMC may prove to be a satisfactory and cost-effective alternative to existing viscoelastic agents in small-incision cataract surgery.

We thank Mr T. Booth of the electron microscopy unit at the University of Newcastle upon Tyne for his assistance.

References

1. Fechner PU. Methylcellulose in lens implantation. Am Intraocular Implant Soc J 1977;3:180–1.
2. Fechner PU, Fechner MU. Methylcellulose and lens implantation. Br J Ophthalmol 1983;67:259–63.
3. Liesegang TJ, Bourne WM, Ilstrup DM. The use of hydroxypropyl methylcellulose in extracapsular cataract extraction with intraocular lens implantation. Am J Ophthalmol 1986;102:723-6.
4. Eason J, Seward HC. Pupil size and reactivity following hydroxypropyl methylcellulose and sodium hyaluronate. Br J Ophthalmol 1995;79:541–3.
5. Storr-Paulsen A. Analysis of the short-term effect of two viscoelastic agents on the intraocular pressure after extracapsular cataract extraction: sodium hyaluronate 1% vs hydroxypropyl methylcellulose 2%. Acta Ophthalmol (Copenh) 1993;71:173–6.
6. Dada VK, Sindhu N, Sachdev MS. Post-operative intraocular pressure changes with use of different viscoelastics. Ophthalmic Surg 1994;25:540–4.
7. Assia EI, Apple DJ, Lim ES, Morgan RC, Tsai JC. Removal of viscoelastic materials after experimental cataract surgery *in vitro*. J Cataract Refract Surg 1992;18:3–6.
8. Rosen ES, Gregory RPF. Is 2% hydroxypropylmethylcellulose a safe solution for intraoperative clinical applications? J Cataract Refract Surg 1986;12:679–84.