J Mater Sci: Mater Med (2007) 18:583–589
DOI 10.1007/s10856-007-2305-5

Preoperative opacification of acrylic intraocular lenses in storage

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Received: 15 November 2004 / Accepted: 1 March 2006

Abstract The preoperative opacification of acrylic intraocular lenses (IOLs) was investigated in order to determine its cause. Opacified IOLs were examined by energy dispersive X-ray (EDX), the buffer solutions were analysed by inductively coupled plasma optical emission spectroscopy (ICP-OES) and the rubber seals used in the bottles in which the IOLs were stored were ashed and tested. The deposit covering the opacified lenses contained a significant amount of zinc, which was absent from fresh IOLs and buffer solution. The source of this was found to be the rubber seals used to seal the glass bottles in which the IOLs were stored. There were two types of rubber seals used, red and grey in colour. The buffer solutions in which opacification had occurred was also contaminated with zinc, but this was only noticeable when using the red seals. This contamination was reproduced by boiling red seals in fresh buffer solution for eighty minutes, to simulate autoclaving. It was concluded that zinc from the zinc oxide used as filler in the rubber seals was leaching into the buffer solution and causing the IOLs to become opacified. This was found to be much worse in the case of the red seals than for the grey ones. However, minute crystals were found on the IOLs stored using the grey ones, which could potentially act as nucleation points for postoperative opacification.

Introduction

Postoperative opacification of intraocular lenses (IOL) has been widely reported, although its cause is not yet fully understood [1–16]. However, in some cases IOLs made from the most commonly used material, polymethyl methacrylate (PMMA), have been known to be become coated with a crystalline material during storage. These were stored in glass vessels with Hanks balanced salt solution (BSS$^{®}$), pH 7 – 8 which had been autoclaved at 121°C for 20 minutes at 2 bar pressure. The glass vessels are closed with a rubber seal, which are either red or grey in colour. The problem of preoperative opacification seems to be more common when the red seals are used. This paper presents the results of the analysis of the material and the formation of the crystalline material.

Experimental

Vista Optics Ltd (UK) supplied samples of IOLs with and without opacification. The lenses, buffer solutions and rubber seals were analysed by a variety of techniques. The samples were supplied in glass vials with two different types of rubber closure, coloured red and grey. It was noted that many of the IOLs which had been stored using the red seals were coated with a white crystalline material, whereas those with the grey seals were clear.

Lenses were coated with a 0.02 micron layer of carbon in an Edwards E12E4 vacuum coating unit. They were then examined using a Jeol JSM 6310 scanning electron microscope fitted with a Pentafet Si(Li) X-ray detector. Images were recorded of the coated and uncoated at a variety of magnifications and, each was scanned by energy dispersive X-ray (EDX), the X-ray analysis was performed using an Oxford

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Instruments ISIS 200 system. The magnifications used were limited by the low melting point of PMMA, which limited the magnification to 6000× for the crystalline coated lenses and 500× for the uncoated ones.

Buffer solutions in which IOLs had been stored were tested as supplied and were examined by inductively coupled plasma optical emission spectroscopy (ICP-OES) analysis using a JY-Ultima 2C, and by UV-visible spectroscopy using a Cary 100 UV-visible spectrophotometer, using freshly prepared buffer solution in the background cell. Fresh buffer solution was prepared by dissolving the salts in water in accordance with the standard makeup of BSS® , its pH being adjusted with hydrochloric acid and sodium hydroxide [17]. A potassium bromide disk of the white crystalline material was prepared and analysed by infrared spectroscopy using a Perkin Elmer Paragon 1000 infrared spectrophotometer. The rubber seals underwent acid digestion in accordance with ISO standard 6101-1. Two seals of each type were ashed at 550°C for eight hours. After cooling, the ashes were transferred to a Teflon® crucible. A few drops of concentrated sulfuric acid were added and this was heated to fuming. After cooling again, 5 drops of concentrated sulfuric acid and 5 ml of concentrated hydrofluoric acid were added and the mixture was boiled dry in a fume cupboard. This was repeated twice more and the resulting residue was dissolved in hydrochloric acid, diluted by 66%. The resulting solutions were filtered, made up to exactly 100 ml and analysed for 32 elements by ICP-OES.

Results and discussion

The IOLs stored using the red closures were all coated with a varying amount of a white crystalline material, whereas the ones stores with the grey closures were clear.

Figure 1 shows the lenses under a microscope.

Whilst the opacified lens is almost completely covered by a white material, even the clear lens exhibited a few crystals. SEM analysis showed that this was a crystalline material and is displayed in Fig. 2.

EDX on the bulk surface o the opacified lens detected the following: Table 1: The above results would suggest that the compound contains silicon, oxygen and zinc with small amounts of various metals such as magnesium and aluminium. The buffer solution in which the opacified lens was stored had a small amount of white precipitate floating. This was analysed by UV-visible spectroscopy and by ICPOES.

The UV-visible spectroscopy of the buffer solution, shown in Fig. 3 below, reveals an absorption peak which is somewhat stronger for the red sealed solution than the grey one, which indicates that there is more contamination in this sample. Infrared analysis of the white powder was consistent with that of a silicate compound, with a strong peak at 1012 cm^{-1}, a medium peak at 665 cm^{-1} and a strong peak at 452 cm^{-1}.

Table 1 Composition of surface crystals on IOL determined by EDX

	Atomic abundance (%)	
Element	Crystalline coated	Uncoated
Oxygen	47	48
Magnesium	0.4	0.4
Aluminium	1.0	0.05
Silicon	39	10
Sulfur	0.1	0
Calcium	1.1	0.4
Zinc	5.6	0

Table 2 Composition of used and unused buffer solutions determined by ICP-OES analysis

Element	Fresh buffer solution	Red seal	Grey seal
Aluminium	0.27	0.192	0.828
Boron	0.08	9.9	4.62
Calcium	124	100	111
Potassium	231.6	654	658
Magnesium	30.46	28.7	29.6
Sodium	218.15	197	197
Silicon	0.71	27.3	46.00
Zinc	0.05	70.4	2.47

The ICP-OES analysis revealed the concentrations (ppm) of the elements (Table 2).

All of the elements in the crystals were found in greater abundance in the buffer solutions, than in fresh solution. This solution was in contact with three things, the lens, the glass vessel and the rubber seal. Of these it was hypothesised that the most likely source of the contaminants was leaching from the rubber seals, particularly during the autoclaving process. To simulate this, a red and a grey rubber seal were refluxed for 80 minutes in BSS® and the solution was analysed by ICP-OES. The seals were left in the buffer solution for 32 days and reanalysed. The results are given in Table 3.

Whilst there was no significant increase in the levels of calcium, magnesium, potassium or sodium, the concentration of the other elements did increase, which strongly indicates that the rubber was the source of the contaminants. During the following 4 weeks the concentration of boron, silicon and zinc continued to increase. It should be noted that the particulate matter associated with the red seals was rich in silicon, but that the silicon contamination was significantly greater with the grey seals. This apparent contradiction can be resolved by the effect of the zinc contamination. The solubility of silica is pH dependent [18] and it exists in several different forms, such as monionic, colloidal (polymerised silicic acid) and polymeric [19]. At $pH < 7.0$ the silicon

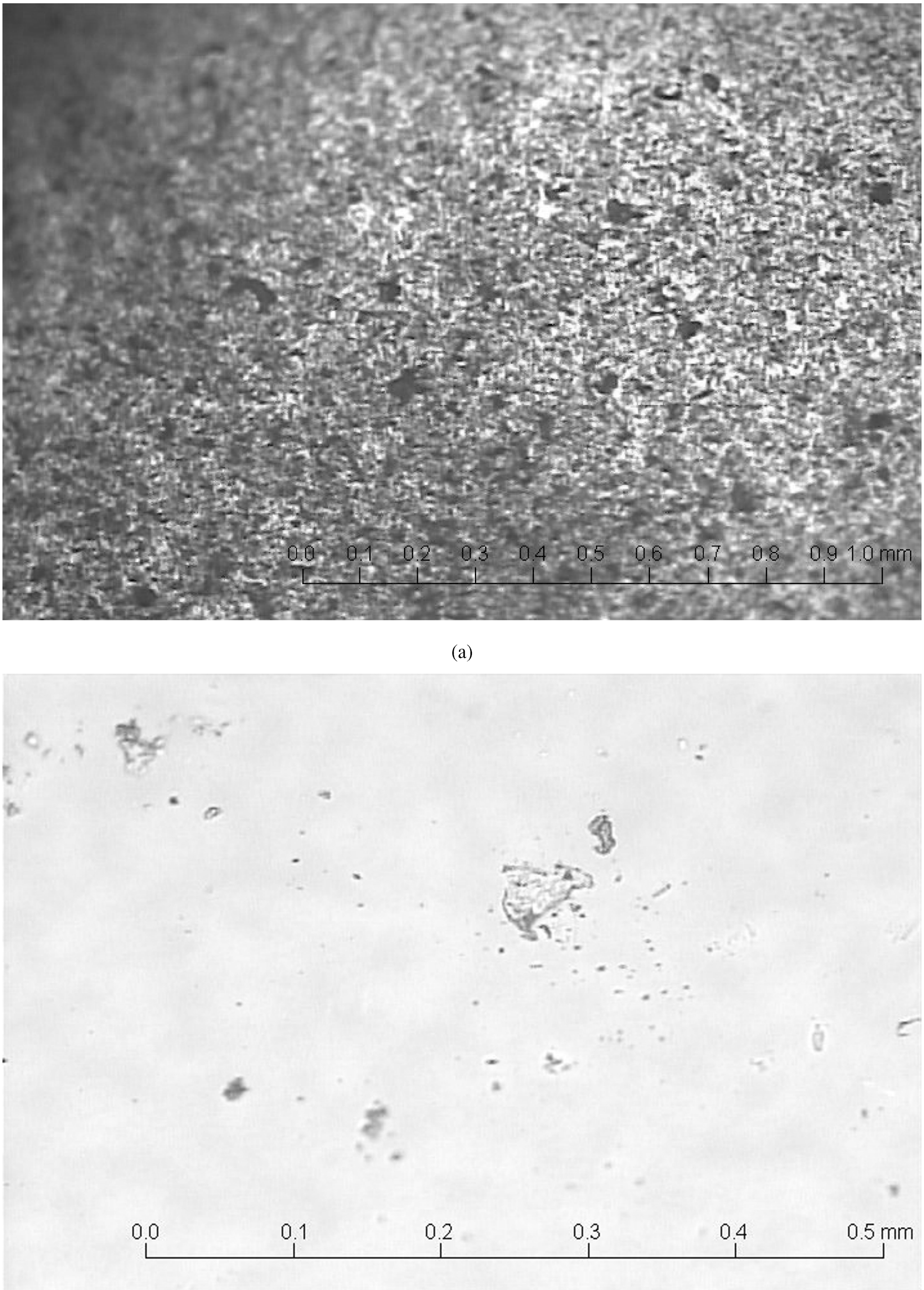
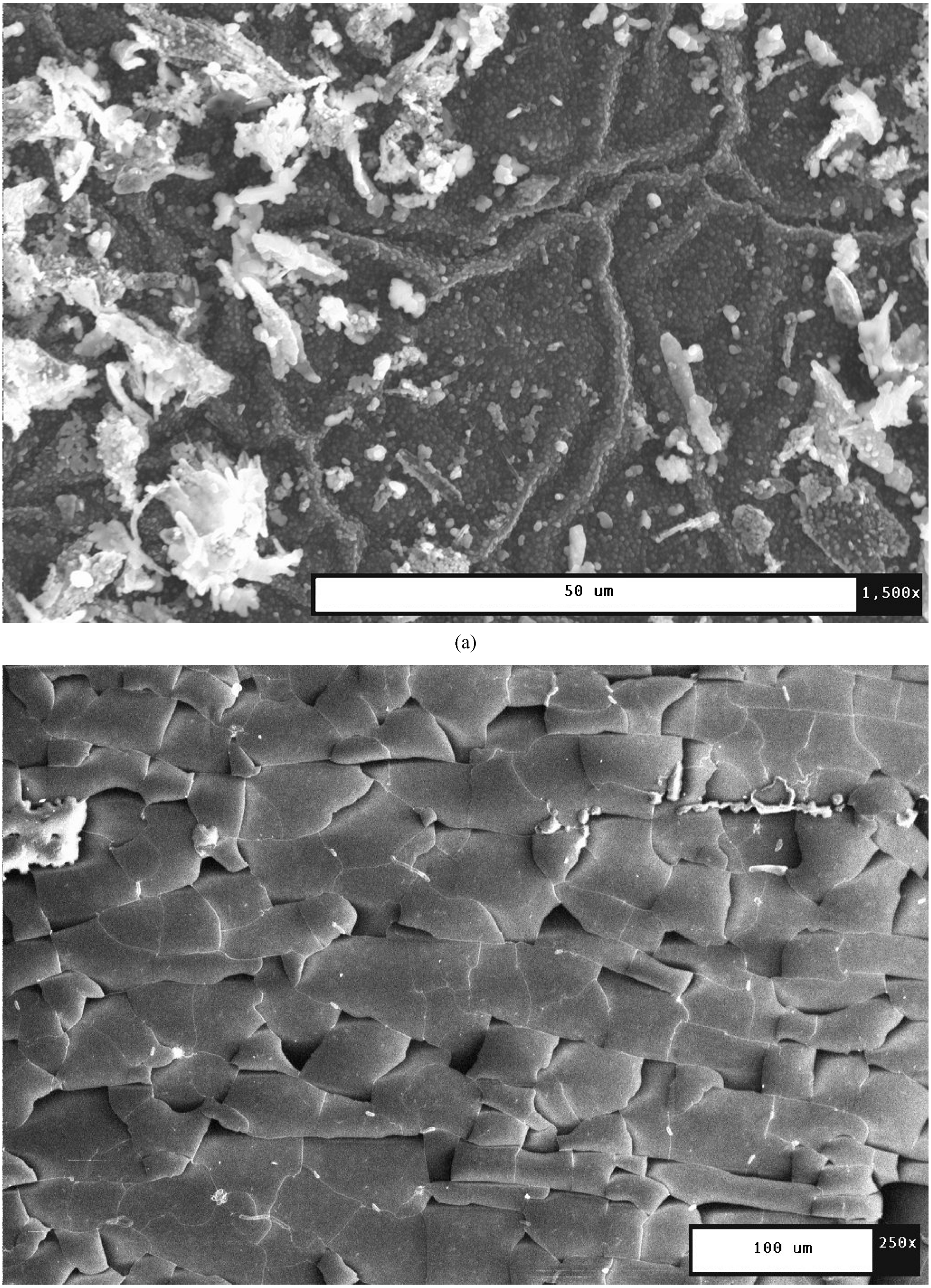


Fig. 1 An opacified (a) and a unopacified (b) IOL.



(a)

(b)

Fig. 2 SEMs of (a) an uncoated and (b) a coated lense.

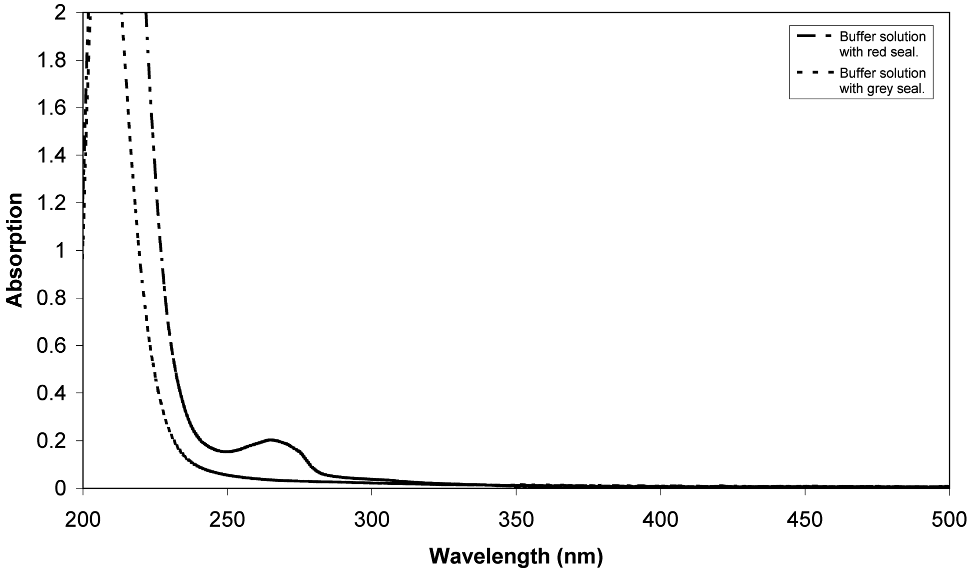


Fig. 3 UV visible absorption spectrum of used buffer solution

Table 3 Contamination of buffer solution resulting from refluxing of rubber seals in balanced salt solution

Element	Fresh Buffer solution	Red seal		Grey seal	
		Refluxed	After 32 days	Refluxed	After 32 days
Aluminium	0.27	0.6	0.41	0.83	0.65
Boron	0.08	0.8	2.28	1.65	2.4
Calcium	124	122	114	125	113
Potassium	426	471	614	461	587
Magnesium	30.5	30.4	29.6	30.3	29.3
Sodium	218	218	192	218	192
Silicon	0.71	12.1	15.9	13.9	16.2
Zinc	0.05	6.3	11.8	0.91	1.02

concentration increases as pH decreases as it becomes silicic acid. At pH > 8.0 silicic acid dissociates into the silicate anion, which is much more soluble, unless [34.3pc] multivalent cations are present, such as calcium, magnesium, iron, aluminium or zinc. At pH < 8.0 the predominant precipitate is SiO2, and at pH > 8.0, silica salts precipitate when multivalent metallic cations are present [20]. Hence, in the samples tested (at pH of 7–8), the precipitate associated with the red seals is likely to be mostly silicon dioxide with some zinc silicate contamination. In the absence of zinc, silicon dioxide does not have anywhere to nucleate; hence it stays in solution. To test this further, the rubber seals themselves were analysed. One rubber seal of each colour was cut in half and examined under a microscope, Fig. 4.

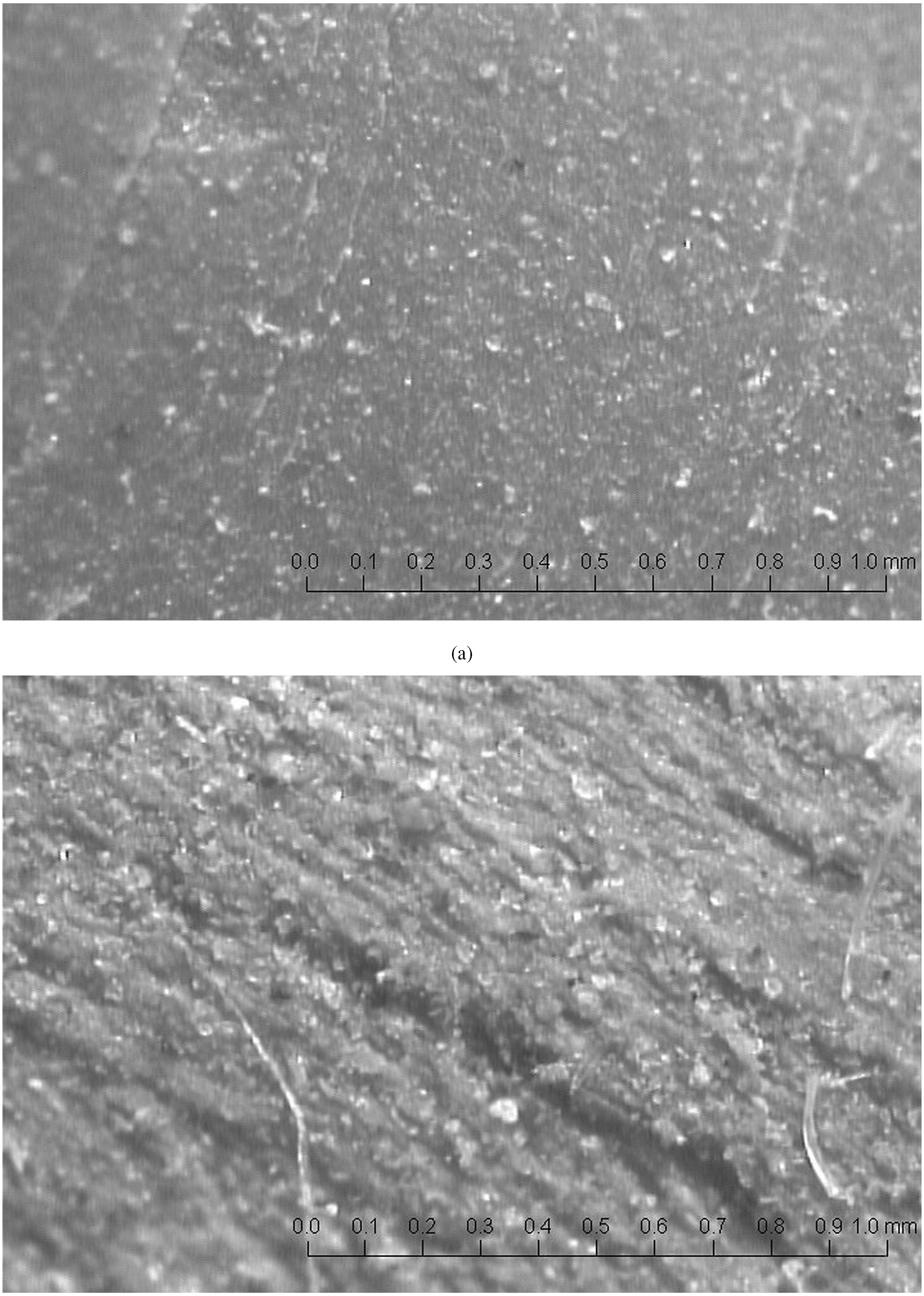
Figure 4 reveals tiny crystal of what appears to be the silica filler, which is the source of most of the silicon contamination (a small amount of the silicon contamination may have come from the glass vessel [20]).

To investigate this further, two seals of each colour were ashed, dissolved and analysed by ICP to produce the results given in Table 4.

Table 4 Elemental content of rubber seals

Sample	Red seals	Grey seals
Element	% concentration (w/w)	% concentration (w/w)
Aluminium	2.74	3.05
Boron	0.024	0.0969
Calcium	0.0566	0.0707
Iron	1.22	0.143
Magnesium	2.29	1.47
Potassium	0.0148	0.0090
Sodium	0.0464	0.0391
Tin	0.0237	0.0163
Titanium	0.124	1.152
Tungsten	0.0445	0.0284
Zinc	1.32	0.775

All of the elements detected on the surface of the IOL were also detected in the bulk of the rubber seal. The iron in the red seal is from iron oxide used to fill the rubber. This, and the other elements not included in Tables 2 and 3 did not appear to leach into saline buffer solution.



(a)

(b)

Fig. 4 Freshly cut (a) red and (b) grey rubber closures

Conclusions

This study has shown that leaching of compounds from the rubber seals is responsible for the formation of preoperative opacification in PMMA intraocular lens kept a common form of storage vial. Aluminium, boron, silicon and zinc contamination were found in the buffer solutions used to store IOLs, but were absent from fresh buffer solution. The problem was much worse for the red seals than for grey ones, which is why opacification is only seen on the IOLs stored in the vessels with the red seals. This was particularly true for zinc contamination, which was only high for the BSS® when the red seals were used. The zinc formed tiny crystals of zinc silicate which acted as nucleation sites around which silicone dioxide crystals formed. Tiny crystals were, however, seen on the surface of the clear IOLs, and are presumed to be of the same material. It seems likely that these can become nucleation sites for postoperative opacification although this has not yet been determined.

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