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Scanning electron microscope analysis of PMMA third generation: a comparative experimental study

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Abstract

Introduction: Polymethylmethacrylate (PMMA) is an inert, biocompatible, rejection-free filler that does not induce infection, necrosis, or tissue damage. It is a polymer used in various diseases and in facial and body sequelae of congenital or acquired diseases, and for aesthetic purposes too. The PMMA manufacturer claims that the product has been improved, purified, and standardized (3rd generation) with rigid microspheres regularity that does not allow phagocytosis, consequently, reducing the inflammatory reaction. **Objective:** To prove this statement, the present study was conducted, whose objective was to analyze the physical characteristics of the PMMA particles distributed by the two Brazilian companies. **Results:** The two samples showed no statistical difference, being virtually the same. **Conclusion:** The surface homogeneity and particle size confirmed the hypothesis of product improvement, which will positively reflect on the clinical results of the product application, this fact can be proven by future studies.

Keywords: Polymethylmethacrylate. PMMA. Implants.

Introduction

Polymethylmethacrylate (PMMA) is an inert, biocompatible, rejection-free filler that does not induce infection, necrosis, or tissue damage (Teixeira et al.,2021) (Bortolozo et al., 2021). The substance called polymethylmethacrylate (PMMA) is a biomaterial used in various diseases and conditions, especially in facial and body sequelae of congenital or acquired diseases, in addition to being widely used for aesthetic purposes (Chacur, 2018) (Chacur et al., 2019) (Chacur et al., 2020) (Bortolozo et al., 2021).

In addition to Brazil, several countries such as the United States, Canada, the European Common Market (which represents 27 countries) China, Peru, Ecuador, Chile, and Argentina, have injectable products with PMMA approved by their corresponding food and drug marketing control bodies. According to Chacur (Chacur, 2018), PMMA has been used in medicine for over 70 years, among its uses are bone cement; contact lenses and intraocular lenses; bone screw fixation; filling of bone cavities and skull defects; and stabilization of vertebrae in patients with osteoporosis or fractures (Frazer et al., 2005).

Lemperle (Lemperle et al, 2003) studied all fillers and ruled out the possibility of severe histological reaction or migration with the use of PMMA, a fact confirmed by Teixeira and collaborators (Teixeira et al., 2021). The safety of PMMA was also studied by Lemperle reaffirming the biocompatibility of the microspheres (Lemperle, 2018).

The study by Hilinski and collaborators (Hilinski et al., 2009) demonstrates improved biocompatibility as a result of the increased size and uniformity of PMMA microspheres. This means fewer adverse events after product placement, providing a permanent volume increase by stimulating the fibroblasts that synthesize and deposit collagen around the non-absorbable microspheres. In a histological study, Lee and collaborators stated that the mixture of PMMA and cross-linked dextran in hydroxypropyl methylcellulose can be safely applied for soft tissue augmentation with longevity greater than twelve months (Lee et al., 2014). (Blanco et al., 2018).

In the Brazilian Consensus about the Use of PMMA (Blanco et al., 2018) 87,371 patients were analyzed, with 71,136 cases of facial implants and 12,285 cases of body implants. From this immense series, we highlight

the occurrence of complications such as granulomas in 0.2%, necrosis in 0.003%, nodules in 0.3%, and local infection in 0.015%. This means that 99.17% of the patients did not experience complications with the use of PMMA.

Along the same lines, Chacur and collaborators published a cohort study, with a 10-year follow-up, in which an analysis of 2,770 cases of gluteal fillings with PMMA is performed, and again the complication rates are very low, nodules 0.21% and puncture site infection in 0.07%, demonstrating the safety of using PMMA, which is currently purified and better prepared (3rd generation) than its predecessor, eliminating several inconveniences from the past. Currently, the injectable products with PMMA marketed in Brazil are Biossimetric and Linnea Safe, both registered with Anvisa, Brazil's regulatory and inspection agency.

The manufacturer claims that the product has been improved, purified, and standardized (3rd generation) with rigid microspheres regularity that they do not allow phagocytosis and, consequently, reduce the inflammatory reaction. To prove this statement, the present study was conducted, whose objective was to analyze the physical characteristics of the PMMA particles distributed by the two Brazilian companies.

Methods

The gel samples containing polymethylmethacrylate (PMMA) were delivered to the company *Todo Mundo Vende Consultoria e Treinamentos* for a microscopic analysis of the products. Sealed samples from 3mL syringes containing 30% PMMA gel were named A and B. The analysis was performed at the Multiuser Laboratory of High-Resolution Microscopy LabMic, Institute of Physics, Federal University of Goiás, Brazil.

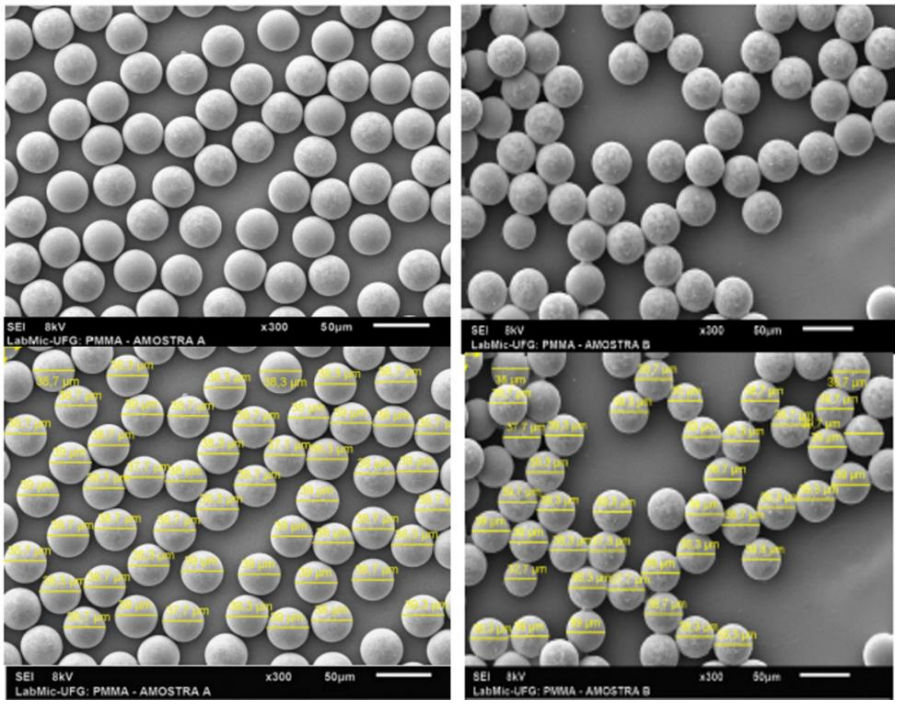
In the analysis, an aluminum sample holder, specific for the Scanning Electron Microscope (SEM), and a glass microscope slide were used. Approximately 0.1mL of sample from the initial part of the ampoule was discarded. Then, on the clean and dry microscope slide, an aliquot of the sample was spread using a disposable spatula to form a thin film. The thin film slide was dried in a silica gel desiccator at room temperature. Subsequently, it was fixed with double-sided carbon tape in the aluminum sample holder and then covered with conductive material, gold, using a system for deposition of gold films, brand Denton Vacuum, model Desk V, and analyzed in the SEM, brand Jeol, model JSM – 6610.

To determine the size dispersion of PMMA particles, images were taken with a fixed magnification of 300 times. The Scandium program, from Olympus Soft Imaging Solutions GmbH, was used to analyze the images and determine the particle sizes. Approximately 3,000 (three thousand) particles constitute an adequate sample for a good particle size distribution statistic. Student's t test was used to compare the samples.

Results

The particles of both products were photographed and measured, **Figure 1** shows the images obtained and the measurements made of product A and product B.

Figure 1. Image of PMMA particles and their respective measurements (samples A and B).



In this study, 1,531 (one thousand five hundred and thirty-one) particles were measured in sample A and 1,522 (one thousand five hundred and twenty-two) in sample B. The result is shown in the size distribution in **Figure 2**.

The **Table 1** shows the descriptive statistics of the PMMA sample size distribution of product A and product B.

The **Table 2** shows the size ranges, the number of particles in the range and their respective percentages in relation to the total number of particles analyzed.

The particles showed regular spherical morphology, as observed in the images in **Figure 3**, obtained with magnification of one thousand times (x1000) and two thousand times (x2000); (a) (b).

Figure 2. Distribution of measurements of PMMA microspheres.

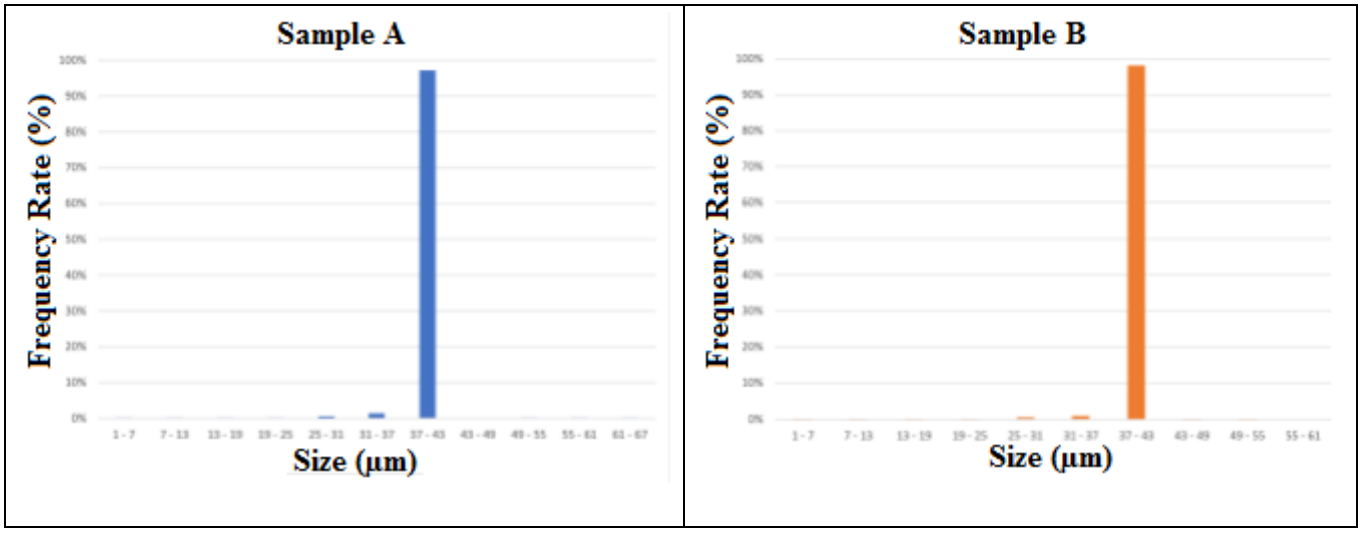


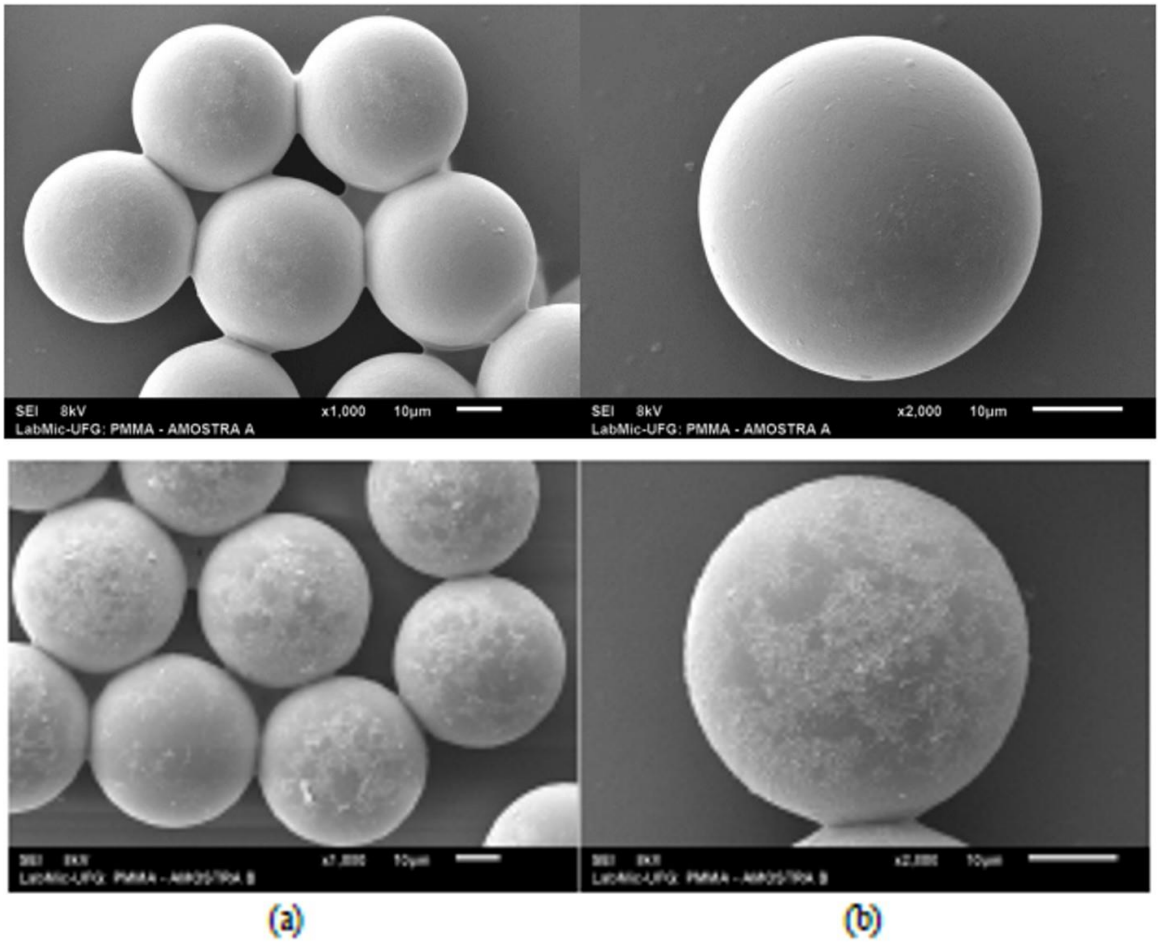
Table 1. Descriptive statistics of the PMMA sample size distribution of product A and product B.

Statistical parameters	Product A	Product B
Particle numbers	1531	1522
Arithmetic mean (µm)	38	38
Standard deviation (µm)	2	2
Minimum measured value (µm)	3.0	6.0
Maximum measured value (µm)	61.7	49.0

Table 2. Shows the descriptive statistics of the PMMA sample size distribution of product A and product B.

PMMA					
PRODUCT A			PRODUCT B		
Size Range (µm)	Quantity of Particles	%	Size Range (µm)	Quantity of Particles	%
1 – 7	2	0.1	1 - 7	1	0.1
7 – 13	1	0.1	7 - 13	1	0.1
13 – 19	2	0.1	13 - 19	1	0.1
19 – 25	4	0.7	19 - 25	2	0.1
25 – 31	9	0.6	25 - 31	7	0.5
31 – 37	22	1.4	31 - 37	14	0.9
37 - 43	1487	97.1	37 - 43	1494	98.2
43 - 49	0	0	43 - 49	1	0.1
49 - 55	2	0.1	49 - 55	1	0.1
55 - 61	1	0.1	55 - 61	0	0
61 - 67	1	0.1			

Figure 3. Polymethylmethacrylate (PMMA) particles with magnifications of (a) x1000 and (b) x2000, of the respective samples A and B.



Discussion

Adequate control of Arteplast/Artecoll started after 1994. Before that, there was a risk of symptomatic granuloma estimated at 2.5%, which was reduced with adequate product control to 0.01%, according to a study by Lemperle and collaborators in the 1990s. In the USA, only in October 2006, the FDA release PMMA, marketed as Artefill (Bellafill, today). Studies and technical improvements in the manufacture of the product led to the current, state-of-the-art PMMA.

The analysis of the particle size dispersion of polymethylmethacrylate (PMMA) in the present study showed that 97.1% and 98.2% (samples A and B) of the particles are distributed in the range between 37 and 43 μm, with a mean diameter of (38 ± 2) μm. Taking into account all measured particles, the overall average diameter is (38 ± 2) μm. The particles showed a regular spherical morphology. There was no statistical difference between the samples (p=0.97).

Such measurements and homogeneous format differ from previous generations of PMMA where a variety of sizes and irregularities of the microspheres were found. The size between 37 and 43 microns prevents phagocytosis, leading to a decrease in the immediate inflammatory reaction and product absorption, in addition to fixation at the implant site, advantages of the new generation of PMMA. One of the products has a slightly rough surface, which, for collagen production, would be a small advantage, to be researched.

Allen et al (1992) followed the organic reactions after implantation with PMMA, in the first 24 hours, neutrophils predominated. In 48 hours, there was a predominance of monocytes, and, in seven days, there was the formation of giant cells against foreign bodies. In two weeks, the cellular response was already moderate; in four weeks, monocytes differentiated into epithelioid cells and in the sixth week, fibroblasts appeared, foreign-body giant cells accompanied by collagen deposition. By the eighth week, the chronic inflammatory cells were dispersed along with massive collagen deposition. In the sixth month, the cellular reaction to the foreign body was stable and a slight cellular response, with a reduced amount of dense collagen and transformation of fibroblasts into fibrocytes.

In the current PMMA, analyzed here, which

demonstrated the increase in the size of the particles and the polishing of the same, a technological advance is reached that allows verifying the non-absorption or migration of the product, and the reduction of possible inflammatory effects, in addition to the formation of a fibrotic capsule, (Teixeira et al., 2021) immense value facts for filler implants.

Conclusion

In conclusion, the two samples showed no statistical difference, being virtually the same. The surface homogeneity and particle size confirmed the hypothesis of product improvement, which will positively reflect on the clinical results of the product application, this fact can be proven by future studies.

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Ethics approval

Not applicable.

Informed consent

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate@.

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