


Consensus Recommendations for the Reconstitution and Aesthetic Use of Poly-D, L-Lactic Acid Microspheres – Comment on the Reason of “Fast Reconstitution” [Letter]

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Dear editor

We are writing to address the reason why injectable poly-D,L-lactic acid (PDLLA; AestheFill) is considered a “fast” reconstitution filler, in relation to the article by Magacho-Vieira et al, titled “Consensus Recommendations for the Reconstitution and Aesthetic Use of Poly-D,L-Lactic Acid Microspheres”, recently published in *Clinical, Cosmetic and Investigational Dermatology*.¹ The authors suggest that the microparticle structure of PDLLA is responsible for its faster reconstitution and more uniform distribution compared to injectable poly-L-lactic acid (PLLA; Sculptra). However, we hold a different perspective.

Injectable PLLA is supplied as lyophilized powders that form a powder cake. Each vial contains 150 mg of PLLA microparticles, 90 mg of carboxymethylcellulose (CMC), and 127.5 mg of nonpyrogenic mannitol. The PLLA microparticles are solid and irregular shaped.² Similarly, injectable PDLLA is also supplied as lyophilized powders but forms into multiple granules. Each vial contains 154 mg of PDLLA microparticles and 46 mg of CMC. Unlike PLLA, the PDLLA microparticles are spherical and feature multiple pores on their surface.² Sterile water for injection (SWFI) is used to reconstitute both products.² Upon reconstitution, neither PLLA nor PDLLA microparticles dissolve; instead, they remain suspended in CMC solutions. In fact, the CMC component in both products plays a crucial role in the reconstitution process. CMC readily dissolves in water to form viscous solutions and serves as a suspending agent for PLLA and PDLLA microparticles. However, CMC tends to form lumps when added to water. The methods used to prevent the formation of CMC lumps differ between the two products^{3,4} (Table 1).

Injectable PLLA employs a pre-mixing method to prevent the formation of CMC lumps when added to water. This method involves mixing CMC and mannitol molecules to ensure that the CMC molecules remain separated before significant

Table 1 The Compositions per Vial, Lyophilized Powder Form, Method Used to Prevent CMC Lumps, and Reconstitution Time in Injectable PLLA and PDLLA

Product	Compositions ²	Form ⁴	Method ^{3,4}	Time ^{1,5}	Descriptions ^{3,4}
Injectable PLLA (Sculptra)	PLLA microparticles 150mg CMC 90mg Mannitol 127.5mg	Cake	Pre-mixing	>24 hours	Mixing CMC with mannitol helps prevent the formation of lumps, but insufficient mannitol may still result in micro-lumps. Extending the hydration time can reduce these micro-lumps.
Injectable PDLLA (AestheFill)	PDLLA microspheres 154mg CMC 46mg	Granules	Agglomeration	10–30 minutes	Agglomeration enhances CMC dissolution by enabling smooth reconstitution steps: wetting, sinking, disintegration, and dissolution.

Abbreviations: CMC, carboxymethylcellulose; PLLA, poly-L-lactic acid; PDLLA, poly-D,L-lactic acid.

hydration occurs. However, due to the limited proportions of mannitol and CMC, complete separation of CMC particles is not achieved, resulting in the formation of CMC micro-lumps. If a large micro-lump is injected into the tissue, it may lead to nodule formation.^{3,4} Increasing the amount of reconstitution water and prolonging the reconstitution time can reduce the number and size of CMC micro-lumps, thereby lowering the risk of nodule formation.^{3,4} This explains why the 2014 consensus recommendations suggested a reconstitution time of more than 24 hours for injectable PLLA.⁵

Injectable PDLA does not contain mannitol. Instead, it utilizes agglomeration technology to prevent the formation of CMC lumps when added to water. Agglomeration is a physical process in which particulate solids adhere to each other through short-range physical or chemical forces. By employing this technology, the reconstitution of injectable PDLA avoids the formation of CMC lumps and micro-lumps. The reconstitution process for these granules involves four key steps: wetting, sinking, disintegration, and dissolution.⁴ This process typically takes 10–30 minutes to complete.¹ As a result, the injectable PDLA is referred to as a “fast” reconstitution filler.

Additionally, post-injection massage may be beneficial after the administration of injectable PLLA,⁵ as it can help break down micro-lumps accidentally injected into the tissue.³ However, it does not appear to be necessary for injectable PDLA.

Disclosure

Dr. JY Lin and Dr. CY Lin are medical directors of REGEN Biotech. The authors report no other conflicts of interest in this communication.

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