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Poly-L-Lactic Acid: Overview and applications

Amany Nassar[1], Dena Ahmed Saleh Sief[2], Reham Farid[1]

1: Dermatology, Venereology & Andrology department, Faculty of Medicine, Zagazig University, Zagazig, Egypt.

2: Dermatology, Venereology & Andrology department, Faculty of Medicine, Tripoli University, Tripoli, Libya.

Corresponding author: Dena Ahmed Saleh Sief

E-mail: dana91gio@gmail.com

Abstract:

Poly-L-lactic acid (PLLA) is a biodegradable, semi-permanent, collagen-stimulating polymer widely used in aesthetic and regenerative medicine. Derived from natural sources such as cornstarch and sugarcane, it combines biocompatibility, mechanical strength, and environmental sustainability. Its semicrystalline structure and slow hydrolytic degradation enable long-lasting results, while its mechanism of action centers on macrophage-mediated breakdown into lactic acid, which activates fibroblasts and promotes type I collagen synthesis. PLLA is FDA-approved for treating HIV-associated facial lipoatrophy and nasolabial fold deficiency, with broad off-label applications including facial volumization, correction of contour deformities, treatment of skin laxity, and body augmentation in areas such as the neck, hands, buttocks, and thighs. Clinical studies consistently demonstrate increased dermal thickness, enhanced skin hydration and elasticity, and durable aesthetic improvement lasting up to two years. Injectable PLLA requires reconstitution and deep-dermal or subcutaneous administration over multiple sessions, while PLLA threads provide both immediate lifting and gradual biostimulation. The safety profile is favorable, with common adverse effects limited to transient erythema, edema, or bruising; nodules or granulomas may occur but are minimized by adequate dilution, proper injection depth, and adherence to post-procedure massage guidelines. Serious complications such as vascular events are rare and avoidable with anatomical awareness and meticulous technique. Contraindications include hypersensitivity to components and a history of keloids, and caution is required in peri-orbital or thin-skinned regions. With growing use in combination treatments such as hyaluronic acid fillers, PLLA has become a versatile, effective, and sustainable option for long-term tissue augmentation and regenerative skin therapy.

Keywords: Poly-L-lactic acid, Collagen stimulation, Tissue augmentation, Aesthetic medicine.

Mechanism and Characteristics

Poly-L-lactic acid (PLLA) is a biodegradable, semi-permanent injectable implant that restores volume and gradually stimulates collagen production **[1].** It is known for its absorbable nature and long-lasting effects.

Indications

FDA-Approved Uses

PLLA is FDA-approved for treating facial lipoatrophy due to antiretroviral therapy in HIV patients, as well as for correcting nasolabial fold deficiencies and other facial wrinkles in immunocompetent individuals **[2].**

Off-Label Uses

PLLA is widely used off-label for volumizing the cheeks, neck, hands, thighs, and buttocks, and correcting chest wall deformities such as pectus excavatum and post-surgical defects. It has shown benefit in improving post-mastectomy "step-off" deformities and breast contour irregularities. It also addresses skin laxity, cellulite, and scars. Optimal outcomes are achieved through multiple sessions spaced 3–6 weeks apart, with correction depending on session number rather than injected volume **[3].**

Chemical Structure

PLLA is a homopolymer in the PLA family, which includes poly-D-lactic acid (PDLA) and poly-D,L-lactic acid (PDLLA) (Figure 3). PLA polymers are thermoplastic aliphatic polyesters valued for their non-toxicity, biodegradability, and mechanical strength. PLLA and PDLA are semicrystalline, while PDLLA is amorphous **[4].**

Environmental and Production Advantages

PLLA is derived from 100% natural resources like cornstarch and sugarcane. Its production avoids petroleum-based processes and uses green catalysts such as cerium trichloride heptahydrate and sorbitol **[5].** Manufacturing PLLA requires less energy, reducing costs. Its structure includes the cyclic dimer lactide LL- and exhibits 30–40% crystallinity. The most stable α form adopts a helical pseudo-orthorhombic conformation, enhancing crystal stability **[6].**

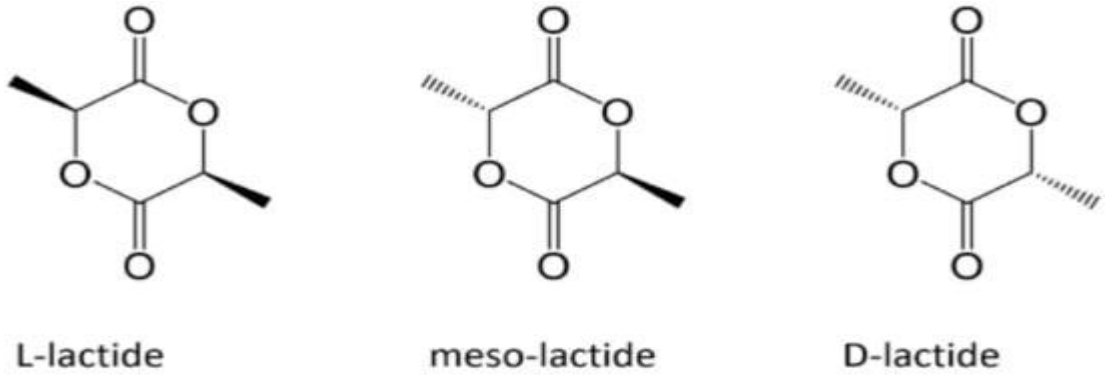

Figure 3. Enantiomeric forms of lactic acid. Reprinted with permission from Frontiers **[7].**

Biological Properties of PLLA

Poly-L-lactic acid (PLLA) is FDA-approved and exhibits lower toxicity than many synthetic polymers. It promotes tissue repair and shows anti-infective properties in vitro and in vivo models **[8].** Its mechanical strength supports long-term regenerative applications. However, its hydrophobic surface may reduce protein absorption and cell adhesion, raising concerns about biocompatibility **[8].**

PLLA degrades via hydrolysis, producing lactic acid—a natural metabolite eliminated as CO_2 and water. This minimizes systemic toxicity. Biodegradation must align with extracellular matrix (ECM) deposition for optimal tissue healing The degradation rate is influenced by crystallinity, strain, and microstructure; lower crystallinity and higher strain increase degradation speed. PLLA's slow degradation, due to its methyl group-induced hydrophobicity, occurs over ~40 weeks in vitro and ~30 weeks in vivo **[4].**

Mechanical and Physical Properties of PLLA

PLLA scaffolds offer high tensile strength (60–70 MPa) and modulus (2–4 GPa), with lower elongation at break (2–6%) compared to polymers like PCL and PDLA. This suits high-load tissues such as bone and ligaments **[8].** Mechanical performance depends on molecular weight, crystallinity, and aging.

Thermally, PLLA is a transparent thermoplastic with a melting point of 170–180 °C and glass transition at ~60 °C. Its mechanical strength can reach ~4.8 GPa, varying by molecular weight. Thermal degradation shortens polymer chains, reducing molecular weight and mechanical stability. The α-crystalline form is the most stable, with randomly oriented C=O dipoles forming a non-polar structure **[9].**

Mechanism of Action

PLLA injection initially causes temporary tissue swelling due to carrier fluid and edema, resolving within 2–3 days **[10].** Once absorbed, PLLA particles trigger a controlled inflammatory response, involving phagocytosis by macrophages. The particles degrade into lactic acid, metabolized to CO_2 and water, while stimulating collagen type I synthesis.

About 50% of the material degrades in 6 months, with collagen-stimulating effects lasting 12–24 months. Neutrophils, macrophages, and fibroblasts contribute to breakdown via enzymes like acid phosphatase and lactate dehydrogenase **[11].**

Applications of PLLA (Injectable and Threads)

Aesthetic and Regenerative Uses

Poly-L-lactic acid (PLLA) is widely applied for tissue augmentation, correction of skin laxity, and collagen regeneration in the neck, chest, buttocks, abdomen, arms, thighs, knees, and hands **[12].** It has been used in facial rejuvenation for over 18 years, addressing volume loss, contour shaping, wrinkle correction, and HIV-associated facial lipoatrophy **[1].**

Clinical Effectiveness

Li et al. [13] demonstrated increased dermal thickness after PLLA injection in lipoatrophy patients via ultrasound. In France, a study of 40 lipodystrophy patients showed increased skin thickness from 2 to 6 months post-injection using photographic analysis **[14].** In the U.S., a 12-month study involving 54 patients found a 54.9% increase in skin thickness via caliper measurements **[15].** PLLA has also improved quality of life and facial contours in HIV-related lipoatrophy **[16]**.

Physiological Skin Benefits

PLLA enhances skin hydration, elasticity, and reduces transepidermal water loss. It also improves erythema, pigmentation, pore size, smoothness, and brightness, primarily through collagen proliferation **[17].**

Comparison with Other Fillers

Hyaluronic acid (HA), first isolated in 1934, offers up to 1 year of effect due to cross-linking but is inactive and requires repeated injections. HA can cause cysts, contour irregularities, and the Tyndall effect, particularly in superficial areas like the glabella and forehead **[18].**

Fat grafting has a survival rate ranging from 20%–80% **[19].** However, over-injection to enhance survival may lead to embolism, deformity, fat necrosis, or calcification. Fat gel injections are useful for static wrinkles but are labor-intensive and controversial **[20].**

Safety Profile of PLLA

Unlike HA or fat, PLLA lacks cross-linkers, minimizing embolism risks even with accidental intravascular injection. No embolism cases have been reported in non-HIV patients. Only one embolism case in an HIV-positive patient on long-term antiretroviral therapy was documented in 2012 **[21].** Thus, PLLA is considered extremely safe in this regard **[22].**

Combination Therapy

PLLA is now often combined with HA. HA can volumize deeper fat compartments and sub-SMAS layers, while PLLA refines superficial layers, enabling multi-level facial rejuvenation **[23].**

Table 1. Applications of PLLA **[12].**

Applications of PLLA			
Tissue augmentation	Body plasticity	Correction of skin relaxation	Collagen regeneration

PLLA = Poly-L-lactic acid.

PLLA Administration and Dosing

Formulations and Reconstitution

PLLA is commonly available as 150 mg of lyophilized microparticles per vial, totaling 367.5 mg with excipients like sodium carboxymethylcellulose and mannitol **[24].** Other brands offer 125–130 mg per vial. Reconstitution typically uses 5–8 mL of sterile water for injection (SWFI); up to 9 mL is now acceptable to reduce nodules**.** An optional 1 mL of 2% lidocaine improves comfort. Hydration should last 2–4 hours, ideally 24–72 hours for better particle dispersion **[25].**

Reconstituted PLLA is swirled gently (never shaken) and may be stored up to 48 hours at room temperature or 3–4 weeks in refrigeration (bacteriostatic water only). It must not be reused or frozen **[26].**

Injection Technique

PLLA is injected into the deep dermis, subcutis, or supraperiosteal plane using 25–26G needles or cannulas. Common techniques include linear threading, fanning, and cross-hatching. One vial per facial side per session is typical. Patients usually require 2–4 sessions spaced 4–6 weeks apart **[27].** Post-injection massage follows the 5-5-5 rule: five minutes, five times daily, for five days **[28].** Ice can be used for edema or discomfort.

Clinical Results and Safety

PLLA should not be overcorrected, especially in mobile areas, as its effect is gradual. Collagen formation begins after 2–6 months and may last over 2 years **[3].** PLLA is best for those seeking natural, long-term correction of atrophic scarring and lipoatrophy.

Injectable PLLA

Mechanism of Action

Injected PLLA first creates a transient volume effect due to water. Its microparticles then induce a mild inflammatory response, activating fibroblasts and stimulating collagen over months **[2].**

Indications

PLLA treats facial volume loss, midface hollowing, nasolabial folds, jawline softening, and is FDA-approved for HIV-related facial lipoatrophy. It is also used for laxity in the face, neck, décolleté, and arms **[25].**

Injection Protocol

Reconstitution and injection follow standard protocols using 26G needles. Post-procedure massage (5-5-5 rule) prevents nodules and ensures even distribution **[10].**

PLLA Threads

Mechanism of Action

PLLA threads offer mechanical lift and biostimulation. Once implanted subdermally, they lift tissue immediately and stimulate neocollagenesis and elastin production over time **[10].**

Indications

Ideal for mild-to-moderate sagging in the jawline, neck, cheeks, and brows. Threads enhance contour and elasticity through collagen induction **[12].**

Procedure

Threads are placed using a cannula or needle in a vector pattern without requiring post-procedure massage. Effects are visible immediately and improve gradually **[12].**

Patient Considerations

- **Pregnancy & Lactation**: Not studied; use not recommended **[29].**
- **Pediatrics**: Safety not established in <18 years **[1].**

- **Elderly**: PLLA helps counteract age-related collagen decline and photoaging by stimulating new dermal collagen **[30].**

Adverse Effects

The most frequent side effects of PLLA are local injection-site reactions, including erythema, edema, and bruising, typically resolving within 7 days **[13].** Deep dermal injection and strict aseptic technique reduce risks. Ice application and sun avoidance are recommended post-procedure.

Hypersensitivity reactions may occur due to PLLA's foreign nature. Skin prep and makeup removal are necessary. Skin testing may be done beforehand **[31].**

Nodules and granulomas are linked to low dilution volumes. Using ≥7 mL reduces the risk. A post-injection massage regimen (5 minutes, 5 times daily, for 5 days) and deeper injection of small aliquots are advised **[1].**

Early nodules can be managed with subcision or sterile water; late nodules may need intralesional triamcinolone (≤40 mg/mL), 5-FU (2–5%), or tetracyclines. Prednisone may help suppress nodule formation **[1].**

Improper injection can lead to lumpiness or filler visibility. Massaging the area helps. Infection is rare but can occur; antiseptics (alcohol + chlorhexidine or chloroxylenol) should be used. For lip injections, HSV prophylaxis (2 days before and after) may be necessary **[32].**

Transient edema, erythema, pain, or heat may occur and typically resolve in 7–10 days. Treatment may include corticosteroids, antihistamines, or NSAIDs. Paraffinoma of the lower eyelid has been reported **[32].**

The most severe complication is vascular occlusion or embolization leading to necrosis. This risk is minimized by slow, low-volume injections, aspiration, and anatomical knowledge. If compromise occurs, apply warm compresses and topical nitroglycerin **[33].**

Drug Interactions

Bleeding risk increases with anticoagulants like aspirin, warfarin, clopidogrel, apixaban, rivaroxaban, and dabigatran. Smoking worsens healing outcomes **[1].** No studies have assessed PLLA interactions with local anesthetics or other injectables. Mixing with other fillers is not advised **[1].**

Imaging Interference

PLLA's radiopacity in humans is unclear, but microparticles may appear on specific imaging techniques **[34].**

Contraindications

PLLA is contraindicated in patients allergic to its components (carboxymethylcellulose or mannitol) or with a history of keloids or hypertrophic scars **[1].**

Boxed Warnings

Intravascular injection can cause ischemia, infarction, blindness, or stroke. If symptoms like visual changes, pain, or pallor occur, injection should stop immediately and urgent evaluation is warranted **[35].** Use in areas of active inflammation or infection should be delayed. Post-vaccine delayed filler reactions have been reported, especially with mRNA COVID-19 vaccines **[36].**

Warnings and Precautions

Safety of varying PLLA dosages, techniques, and concurrent filler use has not been evaluated. Avoid lip vermillion injection. Caution is required in patients with thin skin or during peri-orbital use due to risk of papules and nodules **[13].**

Syringes and needles should be disposed of as biohazards. Post-treatment lasers or other dermal procedures may trigger inflammation if the skin hasn't healed **[37].**

Monitoring

Pre-injection assessment should document asymmetry, volume loss, and keloid history. Baseline photographs are essential. Patients should avoid herbal supplements; anticoagulants should not be stopped. Follow-up occurs at 2–4 weeks. FDA warns against non-approved needle-free dermal filler devices and recommends reporting related adverse events to MedWatch **[38].**

Toxicity

No antidote exists for PLLA. Vascular compromise requires vasodilation strategies like warm compresses and topical nitroglycerin **[1].**

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