

Subcutaneous Fat Lipolysis Injection and Its Efficacy: A Narrative Review and Example of Regentide-LLP53 as Successful Model

Leroy Lucano Sompotan¹

¹Blessme aesthetic
Palangkaraya, Kalimantan Tengah, Indonesia

Publication Date: 2026/03/07

Abstract: The landscape of cosmetic dermatology and non-surgical body contouring has undergone a significant transformation over the last decade, driven by the increasing demand for minimally invasive alternatives to traditional surgical lipoplasty. Subcutaneous injection lipolysis has emerged as a prominent modality for the reduction of localized fat deposits, utilizing biochemical agents to induce adipocyte destruction and metabolic clearance. The evolution of this field is characterized by a transition from broad-spectrum detergent-based solutions to more targeted formulations incorporating biomimetic peptides, glycerophospholipids, and xanthine derivatives. Injection lipolysis represents a robust and safe alternative for body contouring when applied to small to moderate localized fat deposits. As research continues to explore the potential of signaling peptides, Regentide LLP-053 stands as a proven example of how molecular biology can be harnessed to achieve precise aesthetic goals.

Keywords: Injection Lipolysis, Adipocyte, Biomimetic Peptide, Efficacy.

How to Cite: Leroy Lucano Sompotan (2026) Subcutaneous Fat Lipolysis Injection and Its Efficacy: A Narrative Review and Example of Regentide-LLP53 as Successful Model. *International Journal of Innovative Science and Research Technology*, 11(2), 2870-2874. <https://doi.org/10.38124/ijisrt/26feb1455>

I. INTRODUCTION

Biomimetic peptides are widely used to enhance the effectiveness of cosmetic and mesotherapy formulations, including dermal fillers. They play important roles in anti-aging treatments, skin brightening, hair growth stimulation, body fat reduction, and products targeting inflammation, many of which also have pharmaceutical relevance. Over the past decade, interest in synthetic short peptides has grown rapidly, particularly for their potential in disease diagnosis and therapy. Research has shown promising effects of these peptides in areas such as promoting endothelial cell growth and protecting the kidneys from cisplatin-induced acute renal failure (1).

Research findings and everyday clinical practice both suggest that injection lipolysis is a safe and effective option for reducing localized fat deposits. It can be used on its own to treat small to moderate areas of stubborn fat, or alongside surgical procedures to help refine and enhance the overall aesthetic result. For patients who prefer to avoid surgery or who are not suitable candidates for it, this technique offers a valuable nonsurgical alternative to lipoplasty (2).

Two of the most well-known regulators of this process are adrenergic stimulation (such as the effects of adrenaline) and insulin, which plays a central role in controlling fat

mobilization. In the past, hormone-sensitive lipase (HSL) was believed to be the main, rate-limiting enzyme responsible for starting fat breakdown. However, research has since shown that adipocyte triglyceride lipase (ATGL) is actually the key enzyme that initiates lipolysis. In addition, scientists have discovered other important components—previously unrecognized—located at the surface of lipid droplets and within the signaling pathways that regulate this complex and tightly coordinated process (3).

Inside fat cells (adipocytes), the breakdown of stored triglycerides (TAG) into fatty acids and glycerol is a highly controlled process. This usually happens during fasting or when the body needs extra energy. At these times, neuroendocrine signals carefully regulate the activation of enzymes responsible for lipolysis, ensuring that fat is released only when needed (4).

When performed properly, injection lipolysis can reliably reduce small to medium fat deposits. Achieving smooth and even results, however, requires careful patient selection, appropriate dosing and concentration of the injectable solution, precise injection technique, and accurate targeting of fatty tissue only. Attention to these factors is essential to ensure both safety and optimal cosmetic outcomes (5,6).

The emergence of Regentide LLP-053 represents a transition in aesthetic medicine from destructive, non-specific fat reduction toward highly targeted, bio-signaling-based metabolic regulation. Regentide LLP-053 is an independently developed, high-purity oligopeptide designed to modulate the intracellular environment of differentiated adipocytes. Unlike historical lipolytic agents—such as sodium deoxycholate (DC) and phosphatidylcholine (PC), which operate via detergent-like mechanisms to induce cell membrane lysis and necrosis—Regentide LLP-053 functions by mimicking or activating endogenous enzymatic cascades responsible for lipid catabolism (Regentide Notes, 2025.).

In recent years, research led by Asokan and colleagues has found that a small peptide made up of four amino acids—ValHisValVal—derived from soybean protein, can stimulate lipolysis in skeletal muscle cells undergoing apoptosis due to a high-fat diet. Interestingly, this peptide also appears to help regulate tumor necrosis factor-alpha (TNF- α), a pro-inflammatory cytokine that is often elevated in individuals with obesity (5,8). This suggests that beyond promoting fat breakdown, the peptide may also play a role in modulating inflammation associated with metabolic disorders. At the same time, injection lipolysis has emerged as a practical

nonsurgical option for reducing localized fat. For patients who prefer to avoid surgery or are not suitable candidates for lipoplasty, it offers a safe and effective alternative. When used appropriately, it can successfully correct small to moderate fat deposits with minimal invasiveness.

II. LIPOLYSIS INJECTION CONTAINING PHOSPHATIDYLCHOLINE (PPC) AND DEOXYCHOLIC ACID (DC) / SODIUM DEOXYCHOLATE

The use of injectable lipolytic agents to dissolve subcutaneous fat has been popular in several European and South American countries for over 50 years. More recently, a deoxycholic acid (DC) formulation known as Kybella, manufactured by Allergan, received approval from the U.S. Food and Drug Administration for contouring fat in the submental (under-chin) area (9). Numerous studies have evaluated the effectiveness of phosphatidylcholine (PC), deoxycholic acid (DC), and combinations of both, sometimes enhanced with additional agents such as L-carnitine, vitamin E, collagenase, hyaluronidase, and isoproterenol. Overall, these studies have reported promising and encouraging outcomes, particularly in Caucasian populations (10).

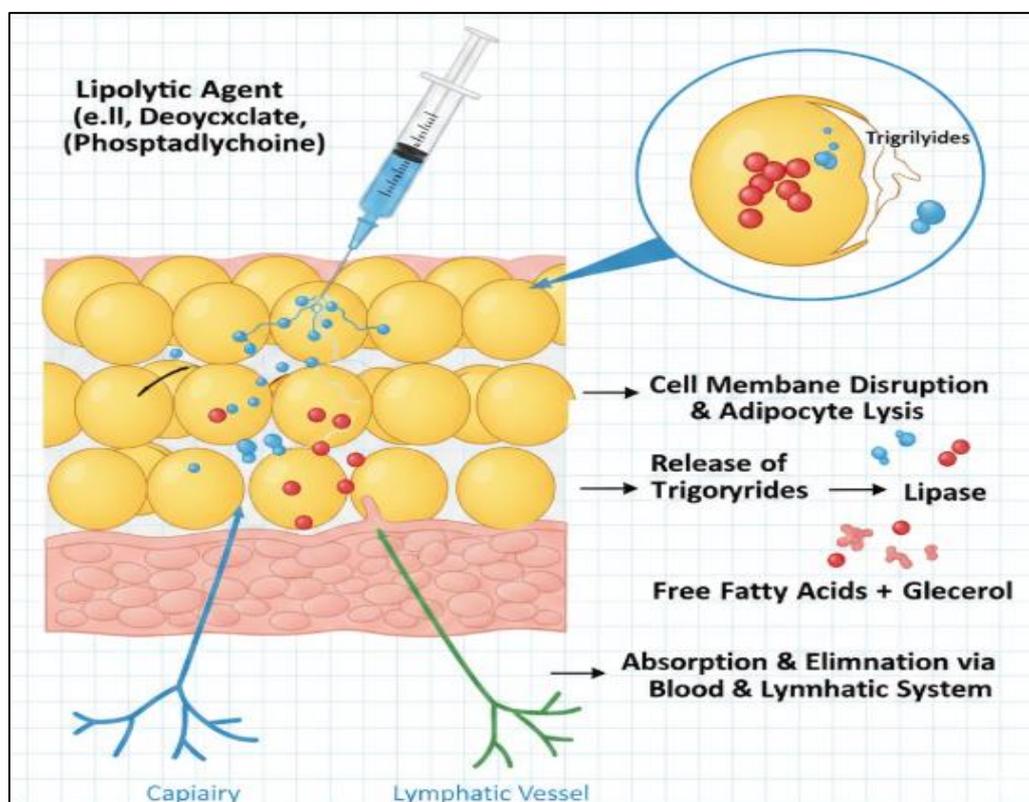


Fig 1 Illustration of lipolytic agent mechanism of action.

Phosphatidylcholine (PC) is a glycerophospholipid that is commonly derived from soybean lecithin. From a biochemical standpoint, it is one of the main structural components of cell membranes. Although PC has long been used in injection lipolysis, its exact mechanism in breaking down subcutaneous fat is still being studied. It is believed that PC may stimulate lipase activity, leading to the breakdown of triglycerides into fatty acids and glycerol. The fatty acids are

then processed by the liver, while glycerol, being water-soluble, is more easily eliminated. Some studies also suggest that PC helps make lipids more water-soluble, thereby facilitating their breakdown and removal (11).

Sodium deoxycholate (DC), on the other hand, is a bile salt that also functions as a laboratory detergent and is used to solubilize PC. Its action appears to be less selective, disrupting

fat cells through its detergent-like properties and leading to cell membrane destruction. Both PC and DC have been used individually for injection lipolysis. However, when combined in a compounded formulation, they appear to have a synergistic effect. Scientific evaluations have shown that when this combination is injected into the fat layer, it causes vacuole formation within adipocytes, leading to cell destruction. The damaged fat cells are then gradually cleared by the body through phagocytosis (12).

Injection lipolysis is best suited for patients with small, localized fat deposits—generally up to about 500 mL in volume. The most favorable outcomes are seen when the excess fat is soft, easily compressible, and evenly distributed. In selected cases, its use can also be extended to treat well-defined lipomas and contour irregularities following liposuction. That said, for a single, well-circumscribed lipoma, surgical removal remains the preferred treatment (11,12).

This technique has also been used to manage small residual fat pockets after liposuction, as well as areas of excess fat retention following fat grafting procedures. In our study, patients presented with similar indications. Most had small, well-defined areas of unwanted fat and preferred a nonsurgical approach over operative intervention (9,10).

III. TRIAL OF LIPOLYSIS INJECTION

Liposuction has long been considered the standard technique for body contouring. In recent years, however, a growing number of noninvasive body-contouring methods have been introduced worldwide, with many published case reports supporting their use. It is important to recognize that both liposuction and injection lipolysis are designed to improve body contours which not to treat obesity itself.

Liposuction is a one-time surgical procedure that typically provides immediate and noticeable results. In contrast, injection lipolysis is a nonsurgical approach that usually requires multiple treatment sessions, and the final outcome may take longer to become fully visible. It is also worth clarifying a common misconception: injection lipolysis is not the same as mesotherapy. Mesotherapy involves injections into the dermal layer of the skin, whereas injection lipolysis delivers medication directly into the subcutaneous fat layer to target adipose tissue specifically (5).

Several studies suggest that phosphatidylcholine (PC) helps make lipids more water-soluble, thereby promoting the activity of lipase enzymes that break down triglycerides into fatty acids and glycerol. Sodium deoxycholate (DC), a bile salt that also functions as a laboratory detergent, is commonly used to solubilize PC. Unlike PC, DC appears to act in a less selective manner, disrupting fat cell membranes through its detergent-like properties and leading to cell destruction. Both PC and DC have been used separately in injection lipolysis, but when combined, they appear to work synergistically. Scientific evidence shows that this combined formulation, when injected into the fat layer, causes vacuole formation within adipocytes, ultimately leading to their destruction. The

damaged fat cells are then gradually removed by the body through phagocytosis (13).

A 2018 study by Thomas et al. reported that 1,269 patients experienced noticeable lipolysis effects following treatment. In this study observations, when comparing consecutive sessions, there was no significant additional change immediately after the second session. Typically, if a marked improvement was seen after the first session, it was followed by a lag phase, during which further reduction continued, but not dramatically enough for patients to clearly notice visually. However, when this study compared measurements from the first session to those at the end of the treatment course, the overall improvement was clear. Similar findings were reported by El Kamshoushy et al. Based on this, we conclude that multiple treatment sessions are important, as the effects of injection lipolysis are cumulative and are best appreciated upon completion of the full treatment plan rather than between individual sessions.

Systemic side effects from injection lipolysis are uncommon and are generally seen only when higher total doses are used, such as in patients receiving treatment in multiple areas during the same session. Reports suggest that these effects are more likely to occur when the total dose exceeds 3 grams. When they do occur, the symptoms are usually mild and related to parasympathetic responses, including dull headache, nausea, diarrhea, or steatorrhea. These symptoms typically develop within the first 24 hours after treatment and resolve within two to three days with simple symptomatic care. Since injection lipolysis is performed as a day-care procedure, it is important to counsel patients beforehand about the possibility of these temporary effects, particularly when the planned total dose of phosphatidylcholine (PC) may exceed 3 grams (6,12,14).

IV. LIPOLYTIC AGENT

➤ *Aminophylline*

Aminophylline is a water-soluble derivative of the xanthine compound theophylline (dimethylxanthine) and retains approximately 80% of theophylline's pharmacologic activity. It was originally developed and widely used as a bronchodilator, typically administered intravenously by adding it to IV fluids. However, in the context of localized injection therapy, aminophylline is given through subcutaneous injections to target specific areas. Although its exact mechanism of action and long-term safety profile in this setting are not yet fully established, several studies have reported favorable outcomes, which has contributed to its broader use in clinical practice. When combined with free hyaluronic acid, known for its strong water-retaining properties, the elimination of aminophylline from the injection site may be slowed. This prolonged local presence is thought to enhance and extend its fat-reducing effects in the treated area (15).

Xanthine derivatives promote fat breakdown through several complementary mechanisms. First, they inhibit phosphodiesterase type IIB, which leads to an increase in intracellular cyclic adenosine monophosphate (cAMP) levels

and subsequent activation of protein kinase which are key steps in stimulating lipolysis. Second, they block adenosine receptors, removing inhibitory signals and further encouraging fat breakdown. Third, aminophylline also exerts a beta-2 adrenergic agonist effect, directly stimulating pathways that enhance the breakdown of stored fat (15).

➤ *Hypotonic Pharmacologic Lipo-dissolution (HPL)*

HPL involves injecting a solution containing fat-targeting substances and lipolytic agents directly into the subcutaneous fat layer. Once injected, these substances cause fat cells (adipocytes) to swell and separate due to hydrostatic pressure, promoting the breakdown and dissolution of stored lipids through their combined effects. The released fat is then absorbed into the lymphatic system and eventually eliminated from the body through urinary excretion (16).

The effectiveness of this method can be enhanced with adjunctive technologies such as ultrasound or low-level laser therapy. In particular, low-level laser therapy has been used to stimulate fat breakdown after findings showed that lipid dissolution can occur at specific energy frequencies. Originally introduced by Dr. Hoefflin, this approach has since been refined and adapted, and it is now applied in various clinical settings for body-contouring treatments (16).

➤ *Glycerol phosphorylcholine*

Choline alfoscerate contains glycerophosphorylcholine, which is a precursor of choline, an essential component of neuronal cell membrane lipids. It plays an important role in maintaining cell membrane structure and also supports neurotransmission by serving as a precursor to acetylcholine. When administered in higher amounts, choline is believed to stimulate fat metabolism. However, its current approval by the FDA is limited to intravenous or oral use. The use of choline as a subcutaneous injection for fat destruction has not been approved and remains outside established regulatory indications (17,18).

➤ *Deoxycholic Acid*

Deoxycholic acid (DCA) acts like a detergent, disrupting the integrity of cell membranes and leading to cell breakdown, as previously described. When injected on its own, it has been shown to cause fat necrosis, with a greater tendency to target adipose tissue compared to other tissues, likely due to its differing affinity for albumin. Although DCA is officially approved for the treatment of moderate to severe submental fat, there is potential for off-label use in other body areas. Despite its growing clinical use, the exact mechanism of action of DCA has not yet been fully clarified. In fact, recent in vitro studies have produced mixed and sometimes conflicting findings regarding how DCA exerts its fat-reducing effects (19).

Although deoxycholic acid injections are officially approved only for reducing submental (under-chin) fat, there have been clinical reports of off-label use for body contouring and even for treating lipomas in various practice settings. In the treatment of jowl fat, clinicians often use smaller injection volumes, typically less than 0.5 cc or dilute the solution with distilled water (rather than saline) to achieve a lower

concentration of around 0.5%, which is about half of the standard 1% strength. These modified approaches have shown encouraging results. In addition, areas along the anterior and posterior axillary lines have also been treated, with some reported cases demonstrating satisfactory contour improvement that was maintained for approximately 3 to 9 months following treatment (20).

V. REGENTIDE-LLP053 AS SUBCUTANEOUS FAT INJECTION

The primary efficacy of Regentide LLP-053 is centered on its ability to stimulate the secretion and activation of three critical lipolytic enzymes: Hormone-Sensitive Lipase (HSL), Adipose Triglyceride Lipase (ATGL), and Perilipin-1 (PLIN-1). In a standard physiological state, triacylglycerols (TAGs) are stored within lipid droplets (LDs) and are protected from lipase action by a protein coating primarily composed of perilipins. The presence of Regentide LLP-053 triggers a specific signaling pathway that facilitates the phosphorylation of PLIN-1. Once phosphorylated, PLIN-1 releases Comparative Abhydrolase Domain Containing 5 (CGI-58), which in turn activates ATGL to initiate the first step of lipolysis, converting TAGs into diacylglycerols (DAGs) (21,22).

Following this initial hydrolysis, HSL is activated and translocated from the cytoplasm to the lipid droplet surface, where it breaks down DAGs into monoacylglycerols (MAGs) and free fatty acids (FFAs). This intricate enzymatic activation ensures that the reduction in adipose volume occurs through metabolic depletion rather than physical destruction of the cell. This metabolic approach is critical for maintaining tissue homeostasis and reducing the inflammatory response typical of necrotic fat-dissolving injections. The specificity of Regentide LLP-053 ensures that it directly acts on the lipid droplets within adipocytes without affecting the structural integrity of surrounding skin cells, such as keratinocytes and fibroblasts (21,22).

The reduction in lipid droplet size is statistically significant ($p < 0.05$). Specifically, treatment with 10 μM of Regentide LLP-053 resulted in a reduction of the mean droplet size to 57.04% of the control value after 48 hours. When the concentration was doubled to 20 μM , the size further decreased to 51.19%, suggesting that the peptide exhibits a potent and scalable lipolytic effect (21,22).

The data confirms that Regentide LLP-053 promotes the fragmentation and reduction of large, unilocular lipid stores into smaller, more metabolically active droplets. This structural change within the adipocyte allows for a higher surface-area-to-volume ratio, facilitating more efficient enzymatic degradation by HSL and ATGL. The implications of this are twofold: first, the rapid reduction in volume translates to visible aesthetic changes in the patient; second, the preservation of the cell membrane avoids the release of intracellular debris, which minimizes the "spicy" or painful sensation often reported with other fat-dissolving products (21,22)

The data indicates that while the peptide effectively reduces lipid content, it does not compromise the viability of the cells themselves. This is a major departure from older generations of "fat-dissolving" injections that caused significant cell death and localized inflammation. Because fibroblasts which the producers of collagen, remain 100% viable during treatment, the clinical outcome is characterized by improved skin elasticity and a lack of the "sagging" effect typically seen after subcutaneous fat loss (21,22).

VI. CONCLUSION

The comprehensive review of current literature and clinical evidence confirms that subcutaneous injection lipolysis is a safe, effective, and reliable non-surgical modality for body contouring. The synergy between phosphatidylcholine and sodium deoxycholate remains the foundational pillar of the treatment, offering a dual-action mechanism that combines direct adipocyte destruction with metabolic stimulation and lipid solubilization. When performed by a skilled practitioner with a deep understanding of subcutaneous anatomy and biochemical mechanisms, injection lipolysis offers a powerful alternative to surgical intervention for small to moderate localized fat deposits. The review of current literature and clinical data supports the use of Regentide LLP-053 as a premier solution for localized fat reduction and cellulite care. Its ability to produce visible results with minimal patient discomfort and zero downtime marks it as a key technological advancement in the field of non-invasive aesthetic medicine.

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