The Science of Mesotherapy: Chemical Anarchy

The author stresses that to date, the effects of mesotherapy have not been scientifically evaluated. Currently, there is no standardization of dosage and no protocol or treatment algorithm to enable prediction of how much tissue or fat will be “dissolved” with a specific solution in a defined quantity, and injected at a specified subcutaneous tissue depth. (Aesthetic Surg J 2006;26:95-98.)

Proposed as a noninvasive alternative to lipoplasty, a treatment for cellulite, and a tool for body sculpting, weight reduction, and skin rejuvenation, mesotherapy remains a controversial therapy.1 Mesotherapy agents, introduced in Europe and South America, are currently not approved for cosmetic purposes. But in Germany, Lipostabil (Sanofi-Aventis, Paris, France) is approved for prophylaxis and treatment of blood vessel blockages by fat embolism. Lipostabil, also marketed as Flabjab, Lipomelt, Lipodissolve, and Fat-Away (Sanofi-Aventis, Paris, France) is not approved as a cosmetic product for the reduction of fat by the Medicines and Healthcare Product Regulatory Agency of the United Kingdom. In the United States, the Food and Drug Administration (FDA) has not approved any drugs for use in mesotherapy.

Although orally administered reagents are prescribed by physicians practicing mesotherapy, new safety data are required if these reagents are to be injected through the skin. Plastic surgeons have recently evaluated claims and complications associated with mesotherapy.2 The position of the American Society of Plastic Surgeons’ Device and Technique Assessment (DATA) Committee is that patients should be wary of mesotherapy until the safety and effectiveness of the procedure are confirmed. “The problem with mesotherapy is that the whole technique is shrouded in mystery.”3

Mesotherapy involves injecting medications, reagents, and plant extracts into the layers of fat and connective tissue under the skin. The injectables are composed of a wide range of agents used to open blood vessels, non-steroidal anti-inflammatory medications, enzymes, nutrients, antibiotics, and hormones. Multiple scientific claims have been made about how these reagents interact with metabolic changes in individual cells, the dermal region, and systemic systems.

Two major rationales are posited for the decreased adipose deposits following multiple treatments. First, the injected reagents are toxic to adipose and other associate cells, causing permanent removal of fat tissue. Cellular necrosis has been documented in some mesotherapy subjects (based on clinical observations). Second, for temporary decrease in fat stores, there is a more subtle mobilization of internal fat within the adipocyte. These unsubstantiated claims state that mesotherapy targets beta receptors for fat release in the adipocytes, increases local metabolism, aids in the reabsorption of fat into circulation, and accelerates fat elimination through the gastrointestinal and urinary systems. To date, no published scientific studies support either treatment rationale or indicate whether the effects are temporary or permanent. To the best of my knowledge, peer-reviewed publications reporting on this subject are few, if any. How can such diverse cellular outcomes be associated with one therapy, even if the same reagents are used?

Unveiling a Mystery

Two major chemicals, primary ingredients of Lipostabil, are currently used in mesotherapy: phosphatidylcholine (PC) and deoxycholic acid. Most mesotherapy clinics and associated websites appear to use Lipostabil or a facsimile, alone or in combination with other compounds. Mesotherapy agents vary from physician to physician, as do the quantity and frequency of injections (ie, there is no standardization of dosage). Therefore, no protocol or treatment algorithm is available to enable physicians to predict how much tissue or fat will be “dissolved” with a specific solution, in a
defined quantity, and injected at a specified subcutaneous tissue depth.

**Phosphatidylcholine**

Phosphatidylcholine is composed of a glycerol backbone with 3 attached groups: 2 long chain fatty acids and choline. When PC is ingested, most of it is broken down into choline, glycerol-free fatty acids, and the phosphate group, rather than incorporated intact into cellular membranes. In considering mesotherapy, the fate of PC when injected into the skin at high concentrations is not well known.

From a lipidologist’s viewpoint, PC can exist in 3 different chemical forms when injected into an aqueous environment (Figure 1). Phosphatidylcholine, at low molar concentrations, forms lipid bilayers, a chemical organization similar to cell membranes. Under agitation, PC molecules can form discrete vesicle structures that have an aqueous-containing interior core. At higher concentrations ($4 \times 10^{-10}$ M), known as critical micelle concentrations (CMC), micelles form that have organic soluble-containing cores. This is important because released triglycerides from disrupted fat cells cannot be transported by a PC bilayer or a PC vesicle, whereas a PC micelle is capable of solubilizing and transporting triglycerides and free fatty acids. If Lipostabil is injected at 90% (w/v), PC will exist predominantly as a micelle. However, mesotherapists use different solutions, and the chemical form(s) are not known.

Phosphatidylcholine interactions with cell membranes have been examined. Phosphatidylcholine increased the solubility of cholesterol. More importantly, PC-rich lipoproteins are external to the subcutaneous adipocytes as high-density lipoproteins (HDL) that serve as carriers of excess cholesterol from extrahepatic cells to the liver (Figure 2). The mobilization of intracellular cholesterol is well defined and beyond the scope of this review. In the context of mesotherapy, intracellular cholesteryl esters can be mobilized to form free cholesterol, which is then diffused through plasma membranes and carried by HDL. During this process, triglycerides may also be hydrolyzed to glycerol and free fatty acids along with cholesteryl esters. Free fatty acids diffuse through the membrane and are transported via albumin. Therefore, a metabolic pathway that requires PC-rich particles does exist for the reduction of adipocyte fat levels and does

**Figure 1. Physical forms of phosphatidylcholine.**
not involve necrosis. In fact, in several clinical trials evaluating Lipostabil, HDL cholesterol levels increased using dosages ranging from 1.5 g once daily to 3.5 g 3 times daily.\(^7\)

**Deoxycholic Acid**

The second major component in Lipostabil is deoxycholic acid. As a bile salt, high concentrations of deoxycholate are known to have toxic effects on skin and pulmonary systems. From a chemist’s viewpoint, deoxycholate can exist in 2 forms. The first is as a monomer and the second is a micelle \((\text{CMC} = 5 \times 10^{-3} \text{M})\). Using the deoxycholate content advertised in Lipostabil, CMC will not be adequate \((2.0 \text{ g/L vs CMC of } 2.1 \text{ g/L})\) to meet micelle status, and deoxycholate will exist predominately as a monomer if injected alone. However, if injected with PC, mixed micelles or micelles containing both components should be present, and excess deoxycholate would be in the form of monomers. One can predict the possible physical forms using a 3-phase chart (Figure 3). In the extracellular environment, with low concentrations of cholesterol, 4 distinct phases are possible with the formation of micelles, vesicles, and crystals (which can damage cells).

Currently, one can only presume which physical form is presented to adipocytes with the current formulations. It would appear logical that a micellar presentation format may enhance a subtle mobilization of fat from cells, whereas a vesicle presentation, with excess monomers of deoxycholate, may be associated with increased cellular necrosis. Crystal formation is associated with cellular damage. Based on these varied possible permutations of physical forms and tissue responses (mobilization, necrosis, unknown effects) subsequent to injection with known
dietary reagents, the FDA presented serious concerns and questions that remain unanswered.

**Science of Mesotherapy Today: “Chemical Anarchy”**

There is really no mystery today regarding the state of the art for mesotherapy. A form of chemical anarchy exists. There are no clinical data that have been published that include standardized reagents, treatment protocols (including dose/injection, technique/injection, and interval times), appropriate positive and negative controls, and semi-quantitative endpoints. Mesotherapy kits, now available on the internet, include multiple biologic materials and caffeine. Without specific knowledge of the concentrations of each component (plus stabilizers and additives), as well as knowledge of preanalytical handling, no systematic, rigorous clinical trial can be performed to determine the biological mechanism(s) responsible for clinical efficacy and safety. The science of mesotherapy can be advanced only by scientific and clinical research. Mesotherapy may become a unique tool for cosmetic procedures, but only after scientific validation.

**References**


Reprint requests: Spencer A. Brown, PhD, UT Southwestern Medical Center, Director of Plastic Surgery Research, Nancy L. & Perry Bass Advanced Wound Healing Laboratory, 5323 Harry Hines Blvd, Dallas, TX 75390-9132.

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