

Phosphatidylcholine treatment to induce lipolysis

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Summary

The medicine Lipostabil N[®] has been in widespread use in Europe since 2002 by doctors working in the field of esthetics to achieve a reduction in the volume of smaller fat deposits by means of injections into the subcutaneous fatty tissue.

The lipases released from the adipocytes by means of phosphatidylcholine produce a local breakdown of fat that is then discharged over the liver and metabolized via beta-oxidation. The medicine has been authorized for intravenous use in the prophylaxis and therapy of fat embolisms and liver diseases.

Keywords: detergents, lecithins, lipolysis, phosphatidylcholine

History

Phosphatidylcholine was first isolated in Odessa, Ukraine some 50 years ago. This was followed by further research in Germany and Russia. It has been marketed by Sanofi-Aventis for over 30 years and, at present, the substance phosphatidylcholine is registered in 53 countries. Its main application nowadays lies in the intravenous treatment and prevention of fat embolisms in polytraumatized patients in the treatment of metabolic disorders and as a liver-protecting substance.

Facts

Next to sphingolipids, phosphatidylcholine is the most important essential phospholipid in the human body. As such it occurs ubiquitously in the human organism.

In Italy at the end of the 1980s, Dr Sergio Maggiori began to use phosphatidylcholine in the infiltration of xanthelasma with satisfactory results. He presented this method at the 5th International Mesotherapy Congress in Paris in 1988.¹ In 1995 the Brazilian dermatologist, Dr Patricia Rittes, in a successful self-experiment, treated

her lower eye pads by injecting phosphatidylcholine under her eyes.² In Europe, further study of the medication started in 2001, and the first treatments were made by the author in late 2002. In 2003 "Network Lipolysis" was founded in Germany by Ulrich Bunzek and Dirk Brandl and with this started the European investigation of the scientific background of this new esthetic therapy.

Phosphatidylcholine makes up the largest choline (lecithin) reservoir in the body and is found in bile. It facilitates the emulsification of fat into the tiniest particles within the nanosphere, enabling the absorption and transportation of fat. After subcutaneous injections of phosphatidylcholine into fat tissue, the adipocytes burst³ and phosphatidylcholine increases the secretion of triacylglycerol-rich lipoproteins.⁴

The medicine, Lipostabil N is a composition of 70% phosphatidylcholine, which uses deoxycholate 4.2% as solvent and benzyl alcohol 3% as preservative.

All these ingredients burst the membranes of the fat cell, with deoxycholate as the most active part.

Rotunda *et al.* showed that injecting deoxycholate alone produced similar effects as Lipostabil N[®]. This proves only to be true regarding the bursting of the adipocyte membranes, but the following enzymatic reaction, which leads to the dissolution of fat by producing an emulsion of nano-sized monoglycerides that is transported into the liver and metabolized by beta-oxidation, in the citric acid cycle, is only the result of the function of phosphatidylcholine.

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The phosphatidylcholine combination as it is in Lipostabil N[®] has first a lipocyte-destroying effect and then a lipolytic action by liberating a long cascade of fat down-breaking enzymes, which is active over a period of 8 weeks.

Phosphatidylcholine is also known to protect the liver through the regeneration of liver cells in cases of fat liver hepatitis and alcoholic hepatic steatosis.^{5,6} Its effectiveness also helped save the life of a patient with death-cap mushroom poisoning following the administration of high doses of phosphatidylcholine.⁷

More recently, claims have been made regarding the positive use of phosphatidylcholine in AIDS cases,⁸ particularly in the reduction of lipodystrophy – buffalo hump – without the need for surgery.

The lecithin level in nerve cells also determines conductivity and thus represents a key role in the trouble-free workings of brain and nerve functions. An increase in acetylcholine through the addition of phosphatidylcholine has led to the realization that the condition of manically depressive patients (bipolar depression) and even Alzheimer patients can be greatly improved.^{9,10} Clinical trials have also been conducted in regard to dyskinesia, chorea Huntington, Friedreich's ataxie, cortex atrophies, and myasthenia gravis.

Soya phosphatidylcholine improves the serum lecithin levels three times more than choline chloride, which has been used in neurology so far. This produces a significant rise in the acetylcholine level, and in this way phosphatidylcholine found its way to the treatment of the previously mentioned conditions. In the lungs and inner organs, phosphatidylcholine works as a superficially active substance (surfactant) that prevents alveolar collapse at the end of respiration. Contrary to soya-phosphatidylcholine used in lipolysis injections, this phosphatidylcholine contains a high percentage of palmitic acids: a saturated fatty acid. A mixture of 90% phosphatidylcholine and 10% proteins (surfactant proteins SP-A and surfactant protein D) is naturally produced in the pneumocytes during fetal lung development from the 35th week of pregnancy and spreads like a film over the surface of the alveoli; it can be found in the bronchial secretion and in the amniotic fluid. This facilitates the expansion of the collapsed alveoli in the newborn baby and forms part of the protective and self-cleaning mechanism of the bronchial system. In cases of surfactant deficiency, it is, apart from other measures, installed in the bronchial system.

Phosphatidylcholine is the major component of all cell membranes (70% phosphatidylcholine, 30% phosphatidylserine) and the lipoproteins, in particular the high-density lipoproteins (HDLs) that circulate in the blood. It plays an important role in intra- and extracellular metabolic transport by controlling what goes in and what comes out

of the cell again. In cases of phosphatidylcholine deficiency, the cell wall hardens so that both the entry of nutritious elements and the transportation of metabolic products become more difficult. This can create a delay in the cell functions and results in the premature aging of the cell.

Through its high concentration of transport lipoproteins, phosphatidylcholine has a great influence on the regulation of the lipid homeostasis. It activates the L-CAT (lecithin-cholesterol-acyl transferase) so that accumulations of cholesterol consisting of atherosclerotic plaques are dissolved and transported back to the liver. It has been proved that the reabsorption of cholesterol deposits is far more effective through vegetable soya phosphatidylcholine, with its highly unsaturated alpha-linolenic acids, than through phosphatidylcholine from eggs with its saturated fatty acids. Lipostabil N[®] contains the highly unsaturated soya phosphatidylcholine. Phosphatidylcholine also brings about a considerable decrease in triglyceride synthesis and triglyceride levels, a marked increase in HDLs in the cholesterol metabolism, and the suppression of atherosclerotic plaques within blood vessels and their subsequent dissolution.^{13,14} Dr Sam Baxas, at the Medical Center in Binningen, Switzerland, developed a slightly altered formula of phosphatidylcholine and achieved great success in the field of atherosclerosis by dissolving fat deposits inside the blood vessels using this substance. In this case, it is referred to as X-plaques.¹⁵

Phosphatidylcholine, as the most important membrane lipid, also plays an important role as a cause of inflammations through the biosynthesis of prostaglandins, leukotrienes, and thromboxanes. Arachidonic acids could be one of the fatty acids bound at phosphatidylcholine in the membranes. Phospholipase A2 releases arachidonic acids from the membrane lipids. Through cyclooxygenase develops prostaglandin H2, the precursor of all physiologic prostaglandins and thromboxanes. Chemically, phosphatidylcholine is a glycerophospholipid consisting of glycerol (CH₂OH-CHOH-CH₂OH), which has all three carbon atoms attached. Fatty acids have attached themselves to the first two and phosphoric choline has attached itself to the third. One can say that the phosphatidylcholine molecule consists of one head of phosphoric choline, a centerpiece of glycerine, and a tail with two varying fatty acids (R' = fatty acid).

Through the variety of these fatty acids, a number of functional possibilities for phosphatidylcholine in the body arise. The type of fatty acid and the balance between omega-6 and omega-3 fatty acids in phosphatidylcholine can, among other things, also be influenced by nutrition.

Lecithin choline is essential, which means that it has to be supplied to the body through nourishment. As soon as it is absorbed in the cell, it is phosphorylated through

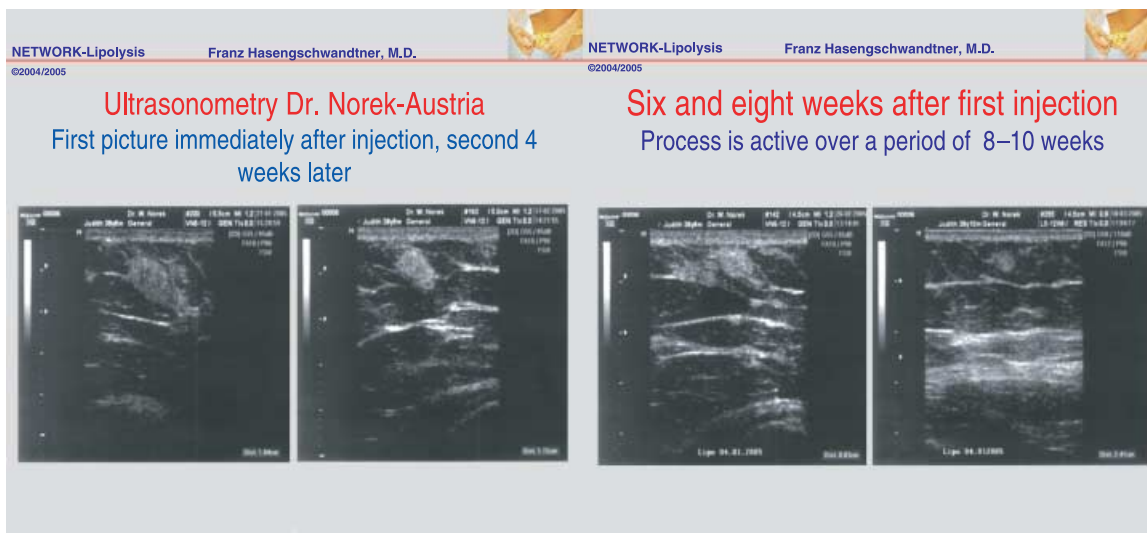


Figure 1 Immediately after injection phosphatidylcholine spreads the size of a table tennis ball. Ultrasound examinations 4 weeks, 6 weeks, and 8 weeks later show the slow reduction of the infiltrate and the reduction of subcutaneous fat thickness. It proves that the process is active over at least 8 weeks.

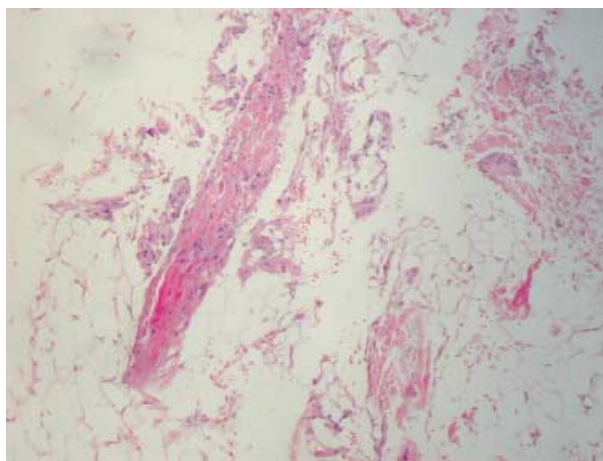


Figure 2 The histological slide was made 10 days after injection-lipolysis and shows exactly the destruction of adipocytes, fibrous deposits, and lipocytes in lysis.

choline kinase and becomes phosphatic choline. Finally, phosphatic-choline, transferases allows phosphatidylcholine to be produced over two intermediate steps.

The second, less important track of phosphatidylcholine synthesis runs over phosphatidylethanolamine, whereby three methyl groups (–CH₃) join the ethanolamine group so that phosphatidylcholine is the result.

When taken orally, phosphatidylcholine is absorbed rapidly with a maximum serum concentration of 8–12 h. The fatty acid on position 2 is separated off through deacylation, thus reaching the intestinal cell as a lyso-phosphatidylcholine,

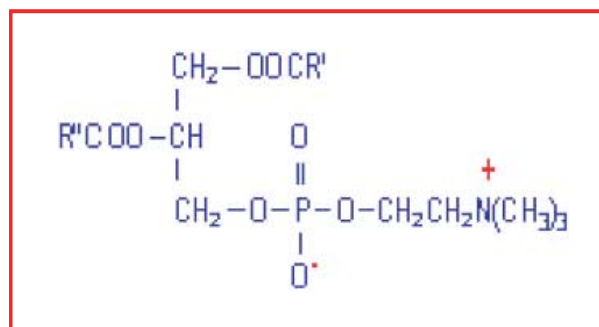


Figure 3 Attached to the glycerol nucleus CH₂OH-CHOH-CH₂OH are the hydrophobis fatty acids (R1 and R2) and the hydrophilic choline-part.

whereas the second position is reacylated and in its complete form as phosphatidylcholine is now available for all tasks in the body. Long-term intake of 30 g/day produced no side effects. Even the manufacturer, Nattermann (Germany), proclaims that even with the highest dosages there are no toxic effects or adverse reactions. In the subcutaneous application of phosphatidylcholine, the deacylation also plays a role in the penetration of the adipocytes.

Through scientific research into the lipolytic mechanism of phosphatidylcholine on adipocytes, it was found that phosphatidylcholine in fatty tissue is hydrolyzed through phospholipase A2 and D, resulting in apolar phosphorylated acids and polar cholines. Cholines are lipotropic substances that function as emulsifiers and are, among other things, components of the phospholipids. Protein kinase C (PKC) causes fat-splitting lipases, i.e., hormone-sensitive



Figure 4 (a) Two treatment sessions, no weight loss, reduction of lower belly of 9 cm. November 2004 to April 2005. Photo by Dr Hasengschwandtner. (b) One treatment session, cheeks, jowls, chin, neck. February–April 2005. Photo by Dr M. A. Palmer, GB.

lipases (HSLs), triglyceride lipase (TGL), diglyceride lipase (DGL), and monoglyceride lipase (MGL). First hydrolyze triglycerides to diglycerides and then to monoglycerides, which are transformed into fatty acids and glycerol. With the help of lipoproteins, phosphatidylcholine is a major component of HDL. These remnants are transported to the liver and are metabolized.

At present, the observation of some 5000 experimental patients within the framework of the Network Lipolysis (www.network-lipodissolve.com) is taking place. These patients represent part of a long-term prospective study that will be carried out over a period of 10 years. An international society for injection lipolysis has already been established (www.injektions-lipolyse.de), as has a society in America (ASAL, American Society for Aesthetic

Lipodissolve (www.asal-meso.com)) and Austria (ÖGIL, www.injektionslipolyse.at). In the meantime, the topic “lipolysis per injections” can be found at every esthetic medical congress.

It should be clear that fat reduction with injection lipolysis is not mesotherapy. Lipolysis injections are subcutaneous injections in a depth of 6–12 mm injected into the subcutaneous fatty tissue. It serves only for esthetic use to dissolve fat. Mesotherapy consists of intracutaneously administered injections in a depth of 1–4 mm and claims to cure hundreds of diseases by injecting smallest amounts of a variety of mostly homeopathic substances (more than 200 are known) into the derma. Mesotherapy was invented by Dr Michael Pistorin in 1952. Mesotherapy and Lipolysis, thus, are entirely different methods.

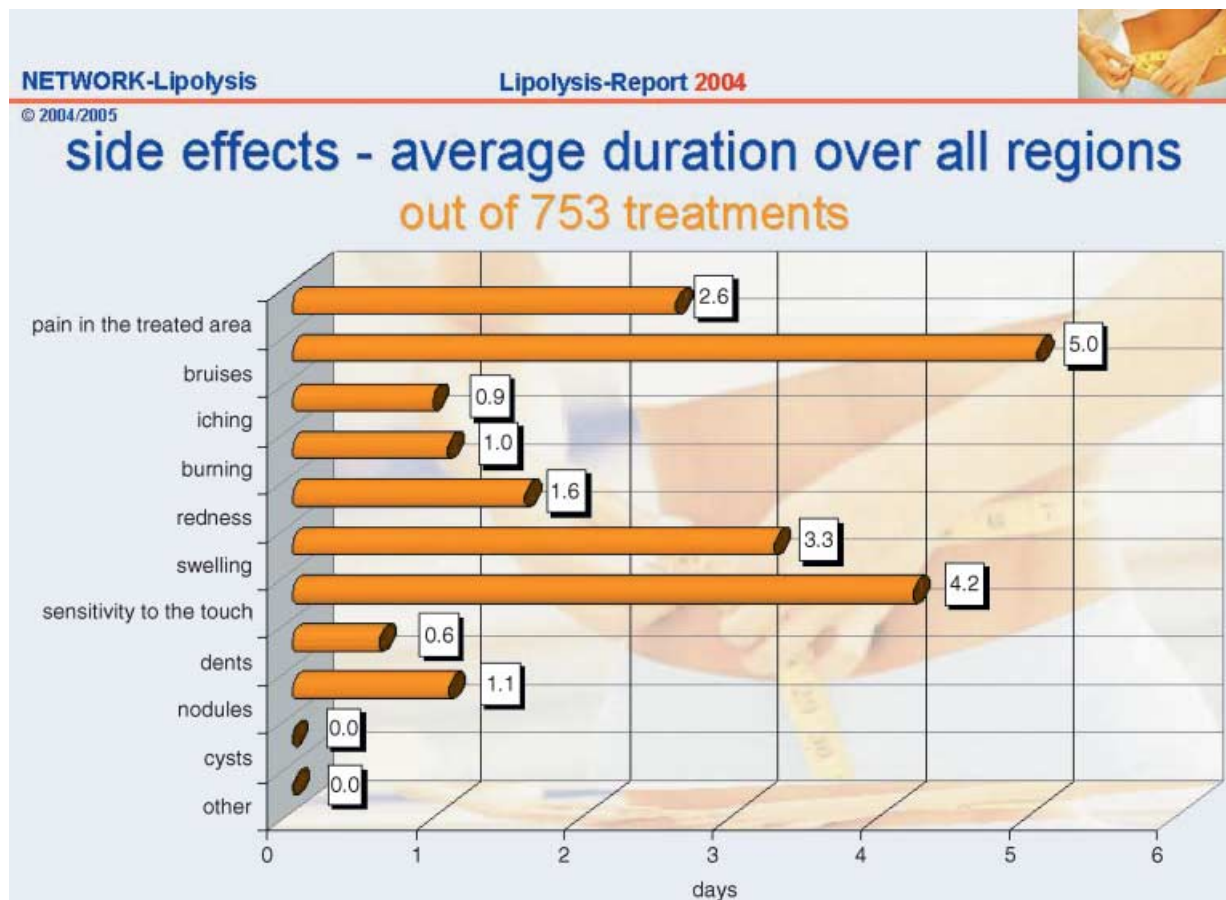


Figure 5 This figure interprets 753 cases of the network's lipolysis report.

By the end of 2004 more than 400 physicians from 29 countries had been trained by Network Lipolysis. Within the framework of Network Lipolysis, further ongoing research investigations and a worldwide exchange of experiences is taking place and a scientific advisory board with scientists from all over the world has been established. It is of importance that any kind of abuse by those who are not authorized to administer injections must be prevented. As far as the medical profession is concerned, one can already say that doctors instructed in the technique and who have been able to learn from the experiences made by their colleagues in the network report satisfied patients, which is not the case with autodidactically working doctors. The only workshops recognized by the General Medical Council in Westfalia, Germany, are to be found in Network Lipolysis. Presently, further scientific research is being planned in cooperation with some universities such as those in Bochum, Nottingham, and Los Angeles.

The use of Lipostabil N[®] or phosphatidylcholine compounds is still, globally, an "off-label" use. Clearly,

this means that although treatment is not forbidden, the responsibility ultimately lies with the administering physician, following significant consultation with the patient. In Brazil, there have been reports of misuse, including the inclusion of unrecognized mixtures by healers, hairdressers, and cosmetic studios with some severe side effects. This led to a ban of the treatment in 2003. The official view of all lipolysis societies like Network Lipolysis and ASAL is that only trained physicians should perform lipolysis therapy.

Discussion

Further scientific investigation of the biochemical mechanism of lipolysis is undoubtedly required. Currently in progress are studies of blood values after lipolysis. It can be anticipated that no negative effect on liver values could be found. Several research groups within Network Lipolysis are preparing the topics for further scientific research and enhancement of the treatment.

Conclusion

Lipolysis by subcutaneously administered phosphatidylcholine is a widespread successful therapy to reduce smaller areas of fat for esthetic reasons. The author, as a recognized expert, has overseen 18,000 therapies that have taken place without the slightest nonexpected side effects.

There are expected local side effects in the injected areas that appear in 100% of the cases and for a short period, such as pain, swelling, itching, bruises, and sensitivity to touch.

For safety reasons, lower eye pads have been eliminated from the list of lipolysis indications by the Network Lipolysis and treatment should only be performed by physicians who are able to make a releasing cut in case of retro-orbital bleeding. Only an existing SOOF (supraorbicular orbital fat pad) would be suitable for injection lipolysis. Injecting a bulging orbital septum, which occurs in a high percentage of all cases, could be dangerous.

Figure 5 interprets 753 cases out of the network's lipolysis report.

After correct treatments, not one single side effect, as it was feared by Rainbow Press and some premature medical statements, was discovered. The nonresponder rate, if using the author developed compound and recommended dosage, wavers between 7% and 1% depending on the experience of the physician. Lipolysis is not a replacement for plastic surgery but a very effective therapy to reduce smaller fat areas in face and body.

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