



## Phosphatidylcholine

By Dr. Franz Hasengschwandtner and Dirk Brandl

In injection lipolysis, we use PPC-DOC (**P**olyenyl**p**hosphatidyl**c**holine-**D**esoxy**c**holic Acid), a combination of substances that has been the subject of intense scientific and medical study. There are more than 2,000 known publications devoted to the subject of essential phospholipids (EPL), as the highly unsaturated phosphatidylcholines (PC) obtained from the soy bean are also known. As well as the more recent studies cited, this article is based in particular on the groundbreaking work "The Essential Phospholipids as a Membrane Therapeutic" of Adj. Prof. Dr. Karl-Josef Gundermann. One remarkable aspect is that this active substance is documented in a very large number and very wide range of different applications, so that readers lacking the necessary scientific knowledge could gain the impression that it is little short of a miracle drug - an impression that this article will, however, seek to put into perspective.

### Phosphatidylcholine and the human body

Phosphatidylcholine has a lot to do with the smallest structural element in the human body, i.e. the human cell, or more precisely with the protective mantle of the cell, the membrane. The cell membrane and the membrane of the sub-cellular organelles is a highly interesting element of the cell, as it is responsible for exchange of the substances transported within the human organism which the cell needs in order to survive. What makes the membrane so interesting is the fact that on the one hand it is pervious to certain substances, while on the other it provides protection for a closed system that leads a life of its own within the cell membrane. The membrane of every cell is made up to a greater or lesser degree of phosphatidylcholine; the membranes of fat cells, for example, contain 70% PC. So it is not surprising that PC occurs naturally in the human body in not inconsiderable quantities.

### Phosphatidylcholine as a membrane therapeutic

Phosphatidylcholine, and especially the form of the substance used by us, namely PPC (polyenylphosphatidylcholine), belongs to the group of the lecithins. Today, the lecithin of PPC is extracted from the soy bean in such high purity that it contains no protein whatsoever and therefore triggers no allergic responses. In contrast to the PC that occurs naturally in the human body, PPC contains in particular two bound unsaturated fatty acids, and it is these in particular that are responsible for its therapeutic effects.

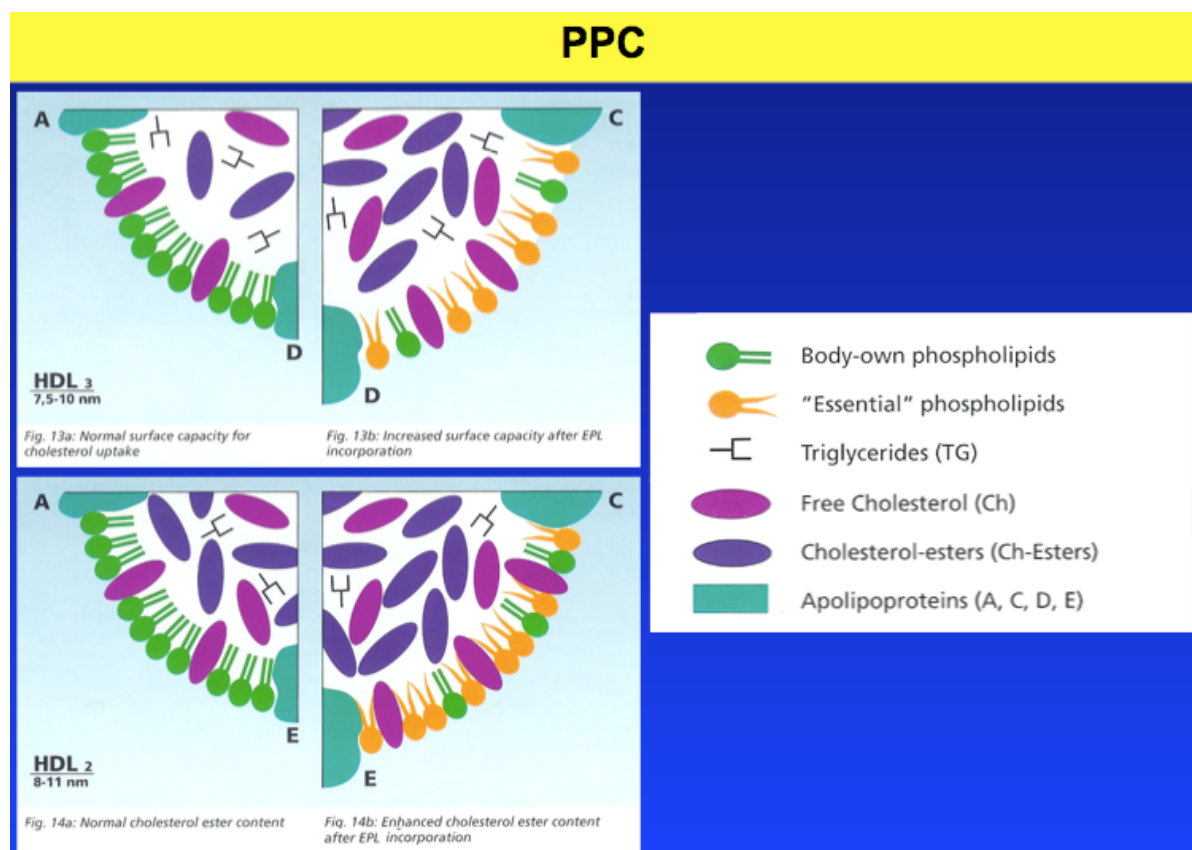
PPC is available in soluble form and tablet form. The soluble form (PPC – DOC [the solvent is desoxycholic acid, a bile acid]) is injected intravenously and has some advantages as compared to the orally administered tablets, especially in terms of the direct availability and purity, while the orally administered form produces its highest blood level around 6 hours after being taken. Moreover, in the case of oral administration, approx. 50% of the PPC is metabolized.

***It is thanks to its affinity to the PC present in the cell membrane that PPC is able to achieve its high therapeutic effect in a large number of different indications.*** Some of the best-known indications for the use of PPC are described in the following.

**Main Function and Importance of PPC:**

- •High energy structural and functional elements of all biological membranes
- •Cellular differentiation, proliferation and regeneration
- •Activity and activation of membrane-bound proteins such as enzymes and receptors
- •Donates polyunsaturated fatty acids as precursors of eicosanoids
- •Emulsifies fat in the blood, the GI tract and in the bile
- •Influences immunological reactions on the cellular level
- •Transfers neutral fat and cholesterol in easier to be metabolized forms

The effect of administering PPC can be clearly demonstrated by the example of lipoproteins with the aid of the illustration below. The PPC is incorporated in particular into the high-density lipoproteins where, because of its two bound, highly saturated fatty acids, it takes up more space in the membrane. The result of this incorporation is enhanced flexibility and functionality of the membrane, which in this example is of the single-layer type.





The general statements made above will now be looked at in detail for various medical conditions:

➤ **PPC as a liver therapeutic**

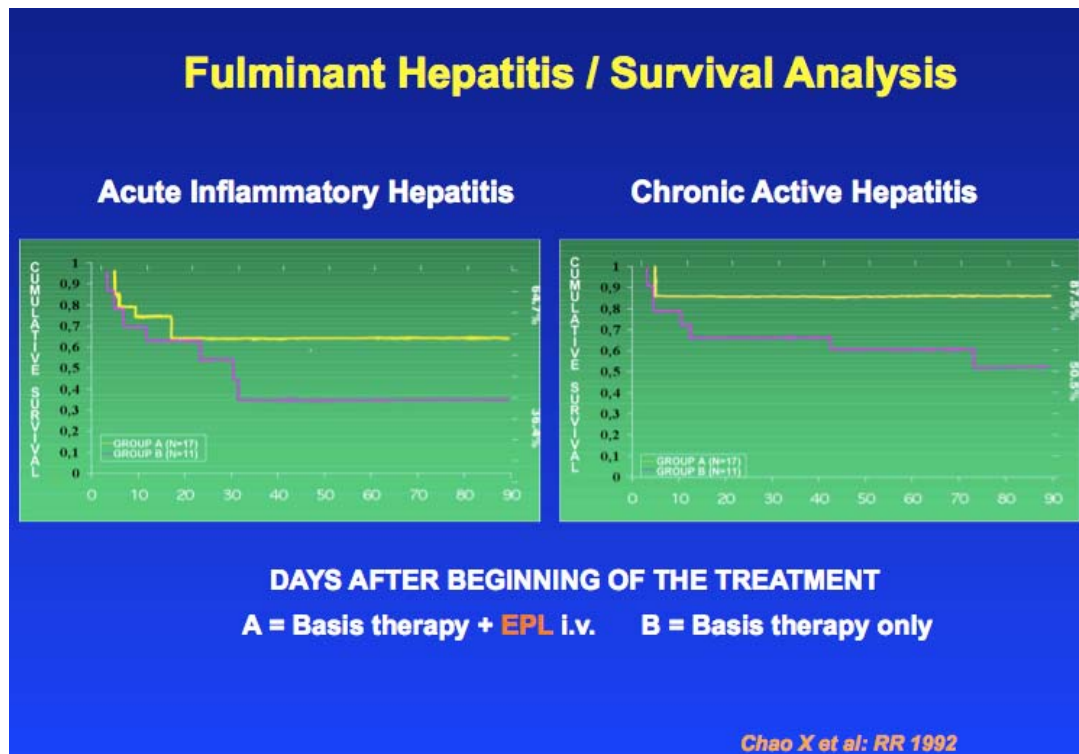
The prophylactic treatment and therapy of various liver disorders is probably the most closely studied area of indications. PPC-DOC is available as a drug in many countries under various brand names, both in tablet form and also in liquid form for administration by injection.

<b>PPC and the regeneration of the liver</b> <b>24 studies performed in total; out of these 13 since 1985 and 9 since 1990</b>						
Author, Year	Ani-mal	Model	EPL Appl.	Biochemical Improvement	RNA/DNA	Cytology / Histology
Barbarino 1990	Mouse	Galactosamine	i.p. s.	<sup>35</sup> S-methion. ↑	↑	-
Saratikov 1990	Rat	Galactosamine	p.o. p.	-	↑	-
Werner 1990	Mouse	Paracetamol	i.v. p.	Protein ↑	-	RER- Volume ↑
Dargel 1991	Rat	Ageing	p.o. c.	-	-	Repair ↑
Holeček 1991	Rat	Part. Hepatect.	i.v. c.	-	-	Mitotic Activity ↑
Holeček 1995	Rat	Part. Hepatect.	i.v. c.	-	-	Mit. Act. & Tissue cellul.
Kropáčová 1995	Rat	Part. Hepatect. + Irradiation	i.p. p., p.+c., c.	Liver Histones ↑	↑	-
Kozurková 1999	Rat	Part. Hepatect. + Irradiation	i.p. p., p.+c., c.	Liver Histones ↑		-
Fomina 1999	Rat	Platidium± CCl <sub>4</sub>	i.g. s.	-	↑	<u>Binuclear cells</u> ↑

As this short table shows, a large number of studies have been conducted with rats and mice and show the wide-ranging effects of PPC intervention on regeneration of the liver. Especially in various types of hepatitis, fatty degeneration of the liver and liver cirrhosis as well as forms of therapy used in the treatment of cancer, such as chemotherapy and radiation treatment, the administration of PPC produces significant positive effects on cell regeneration in the liver.

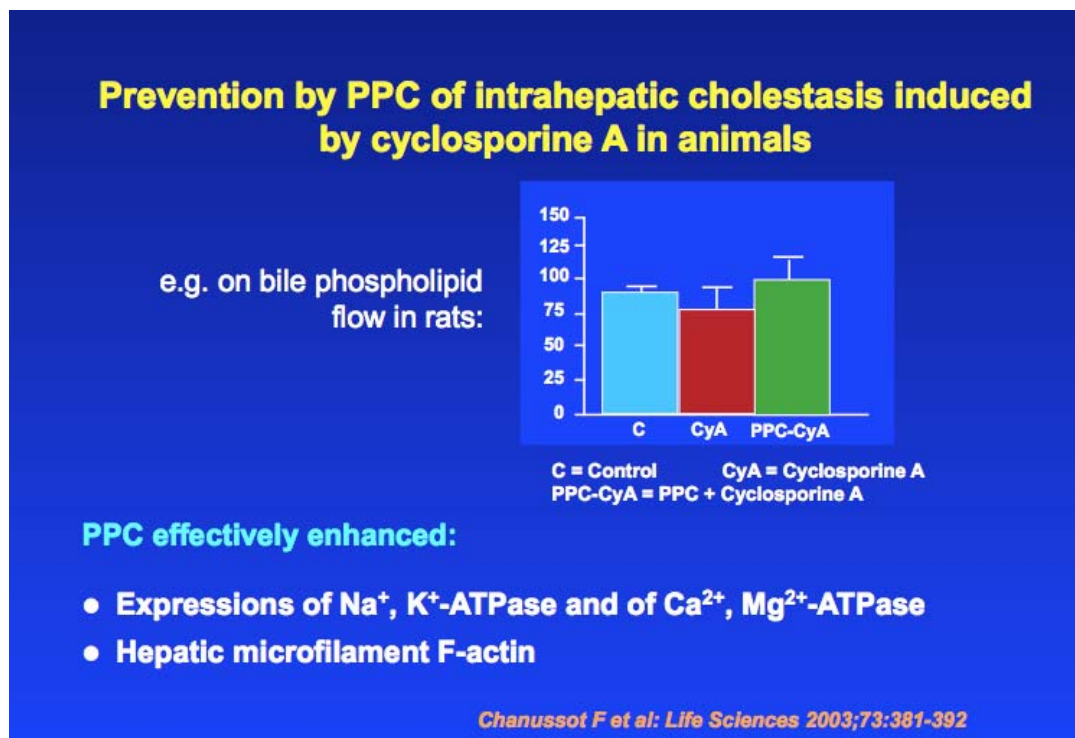


As evidence of this, the following is just one study showing a significantly higher likelihood of survival in the case of patients with chronic and acute inflammatory hepatitis:



➤ **Diseases of the gall bladder**

Also in the case of conditions of the gall bladder, effective improvements triggered by the administration of EPL have been demonstrated in animal trials. One example of this is provided by the study by Chanussot et al. from the year 2003 (Table 4).







➤ **Prevention and therapy of fat embolism**

More than 19 evidence-based pharmacological studies have dealt with fat embolism, a very common indication in Germany, among other countries. There are more than 50 serious clinical publications available on this topic. The following chart shows the improvement indicated by these 50 publications in both the prevention and treatment of fat embolism, whereby the dosage level and duration of administration varied strongly:

### Clinical Results about PPC i.v. and Fat Embolism

PPC i.v. + Basic Therapy				Basic Therapy			
Prophylaxis		Therapy		Prophylaxis		Therapy	
No.	Fat Embolism	No.	Dead	No.	Fat Embolism	No.	Dead
10,986	121	410	57	4,595	138	105	58
1.1 %		13.9 %		3.0 %*		55.2 %*	

\* P ≤0.0001 after Pearson's Chi Square

Fifty papers from 11 countries were published between the years 1959 and 1994;

Dosages: between 0.25 and 9.0 g/day;

Duration of therapy: between a few hours and 31 days

These figures show that supplementing the basic therapy with PPC significantly increases the survival rate in the case of patients with fat embolism.

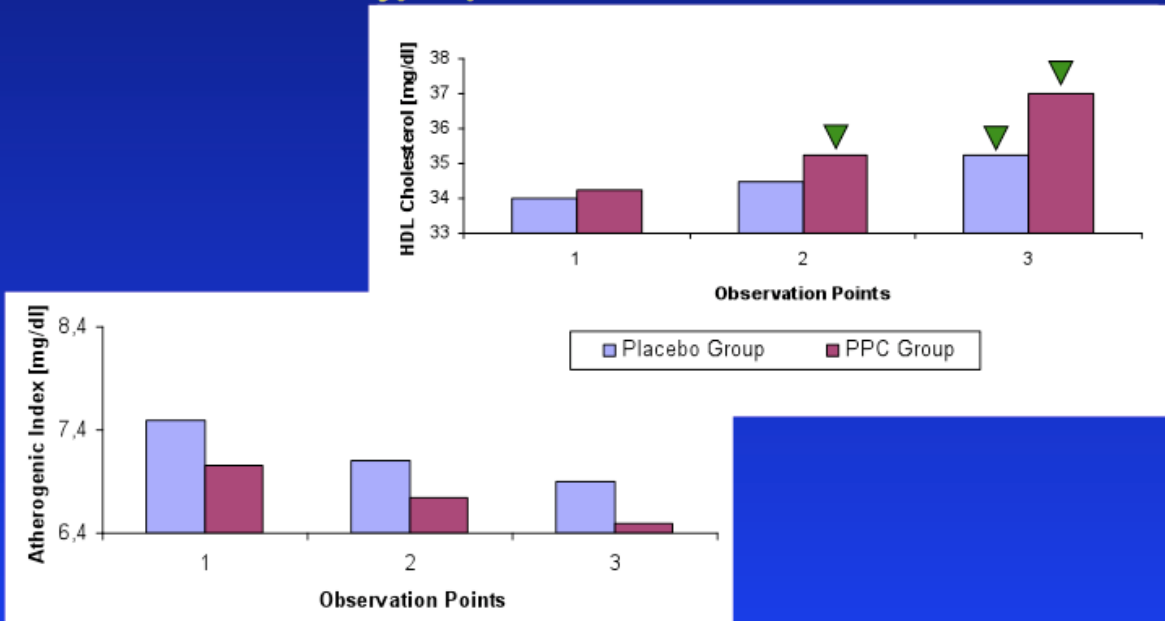
➤ **Arteriosclerosis**

It is not possible in this article to discuss the background to this disease or the theories as to what causes it. However, the formation of so-called atherosclerotic plaques (deposits on the walls of the blood vessels) is of particular importance for the administration of PPC. Arteriosclerosis is a disease of modern civilization that is spreading throughout the developed world; it can cause severe physical damage (stroke, heart attacks, etc.), but is also susceptible to treatment by PPC and damage to the cells in the arteries can be prevented through the administration of PPC.

Of particular interest in this context are 2 studies whose results are summarized in the following 2 charts: a study by a Russian research group (Nikitina et al., 1993) showing the changes to the blood serum in vivo following the administration of PPC, and a further Russian study investigating the atherosclerotic plaques ex vivo after 6 months' administration of PPC in vivo (Orekhov et al., 1996)



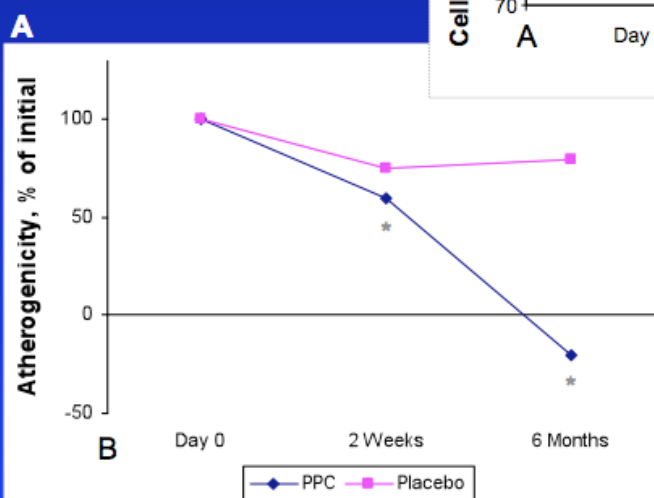
### Serum HDL-Cholesterol and atherogenic index of CHD patients with hypoalphacholesterolemia



- 1 Before PPC administration
  - 2 After 2 weeks of 1g PPC/day i.v.
  - 3 After 6 months of 1.8g PPC/day orally
- ▼ Statistically significant as compared to origin ( $p < 0.05$ )

*Nikitina N et al:  
XIth World Congress of Cardiol.  
Sept 1994 Berlin/Germany*

### Anti-atherogenic (A) & anti-atherosclerotic (B) effect of PPC ex vivo



Patients' sera obtained prior to the therapy (day 0), 2 weeks after i.v. administration of PPC or placebo and 6 months of peroral administration were added to a primary culture of cells derived from human atherosclerotic plaques. Intracellular cholesterol content taken prior to the treatment was assumed as 100%.

\* =  $p < 0.05$

*Orekhov AN et al.: Czyn. Rzyzka 1996; 12/13: 70-76*



➤ **Other effects of PPC on various medical conditions**

Besides the diseases looked at in detail above, the effects of PPC in the case of other medical conditions have also been indicated by studies and should be made the subject of further investigation. These include:

- ✚ Reduction in damage to the liver as a result of artificial feeding
- ✚ Treatment of morbus Crohn and colitis ulcerosa
- ✚ Acute inflammation of the pancreas
- ✚ Treatment of respiratory problems in premature babies
- ✚ Treatment of bipolar depression
- ✚ Also in the case of cancers other than liver cancer, PPC is able to reduce both the harmful effects of the cytostatic drugs used in chemotherapy and also the effects of radioactive radiation on healthy cells

**Phosphatidylcholin and injection lipolysis**

So how does it come about that a combination of substances that is known to have therapeutic effect on the cell membrane nevertheless has the ability to destroy fat cells? This question has not yet been conclusively answered, although certain elements of importance in forming a theory concerning the mode of action are already in place. It is already known, for instance, that the combination of substances acts differently when injected subcutaneously into the fatty tissue than when it is administered intravenously. This is due above all to 2 factors which have already been the subject of investigation: first, the behaviour of the desoxycholic acid, and second, the change in the behaviour of DOC in combination with PPC. DOC is a bile acid that is needed to dissolve the PPC in liquid form. By itself, DOC is highly aggressive, and even in minimal quantities has the ability to destroy cells. In combination with PPC, this aggressiveness is reduced. Nevertheless, a study by Regensburg University has shown that above a certain dosage, cell destruction takes place.

While the DOC destroys the membrane of the adipocytes and breaks down the fat released from the cells into nanoparticles, the PPC promotes the decomposition and removal of the fat to the liver.



The process can be described schematically as follows:

## Mode of Action of (PPC/DOC) in Adipocytolysis I

1. **DOC** adipocyte cell-wall *disruption*  
↓  
glycerides, fatty acids and cholesterol are released
2. **PPC a)** *modifies*  $\beta$ -adrenoreceptor/ $\alpha$ -receptor functioning of remaining adipocytes  
↓  
local enzymatic release of fatty acids  
↓  
the adipocytes shrink in size  
  
**b)** *activates* enzymatic cascade (lipases and LCAT) which emulsifies and degrades the released lipids  
↓  
incorporation into HDL and micelles for reverse transport to the liver

## Mode of Action of Lipobean (PPC/DOC) In Adipocytolysis II

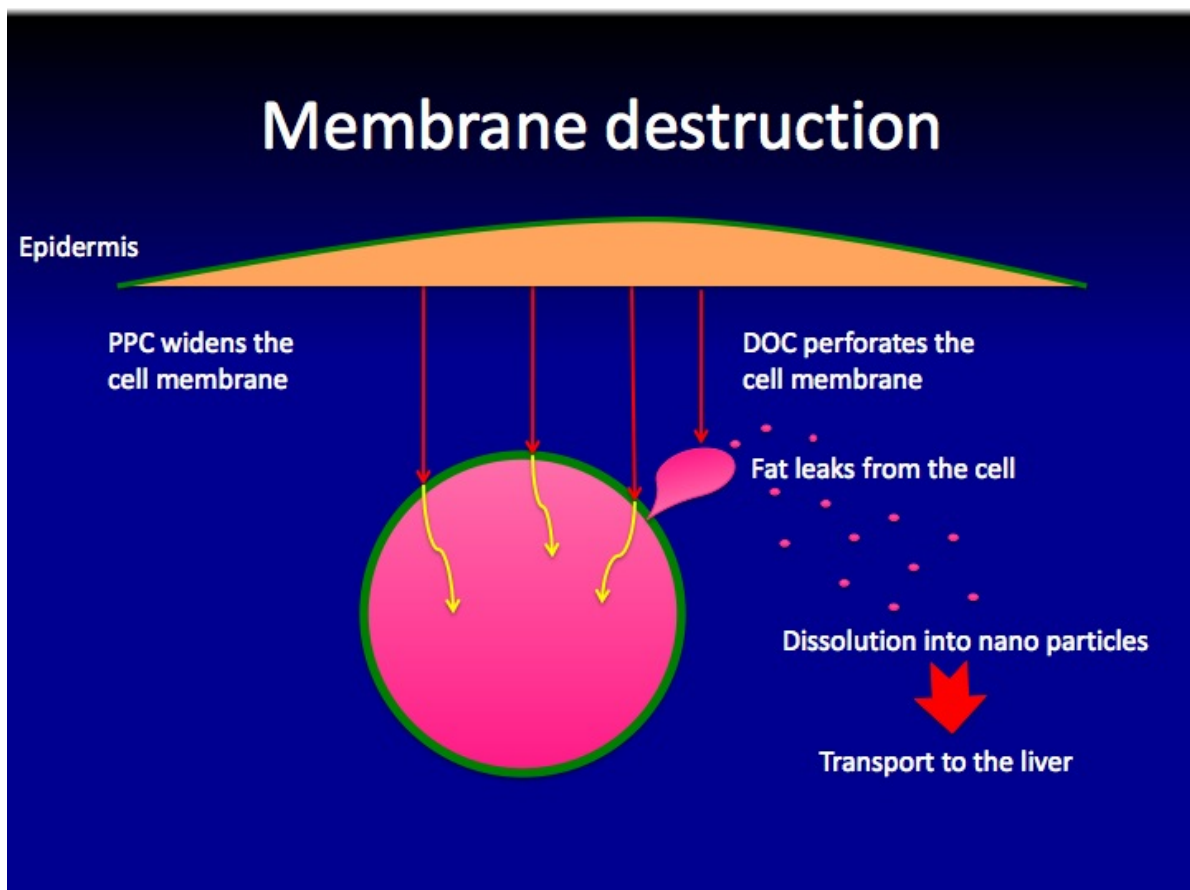
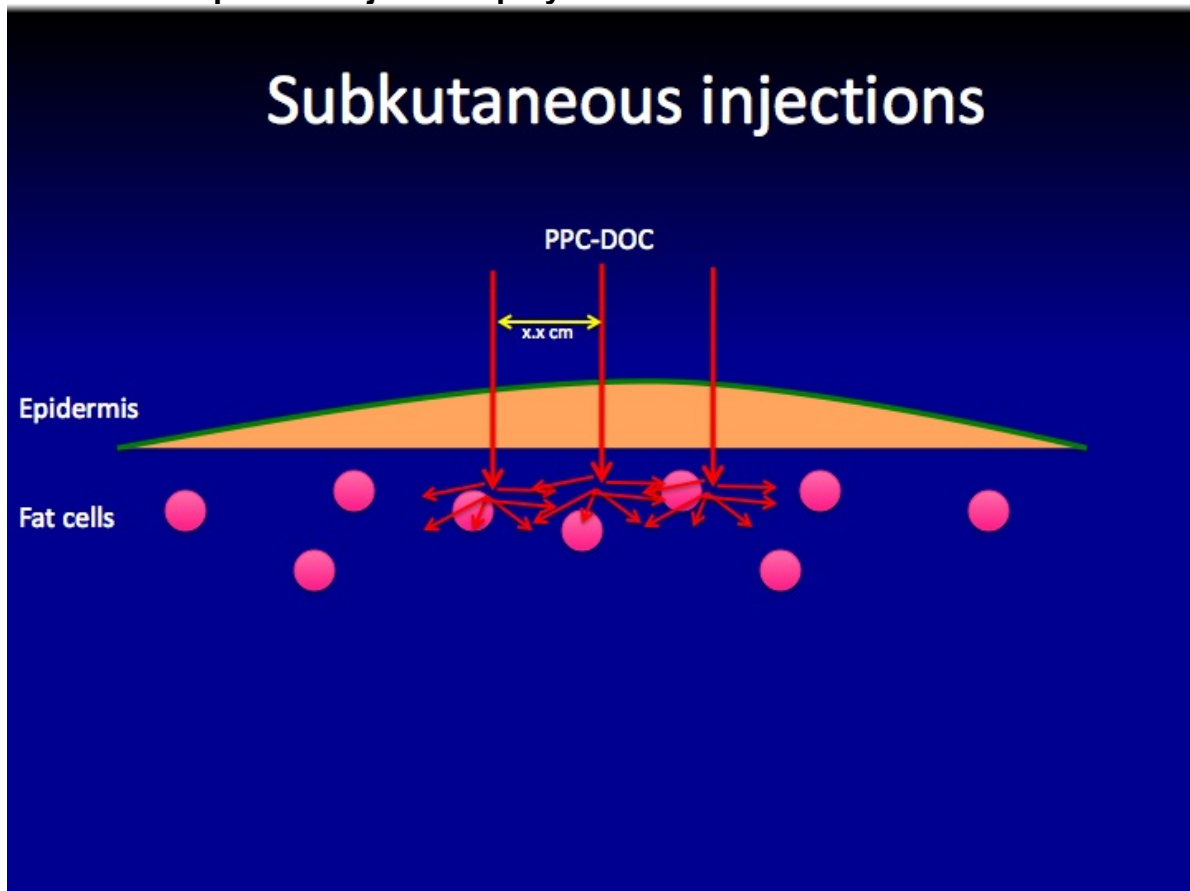
3. Cytokine-induced inflammation  
↓  
Skin retraction  
↓  
Incorporation of fibrocytes  
↓  
Collagen formation  
↓  
Denser, firmer skin character

4. **PPC reduces the toxicity of DOC**



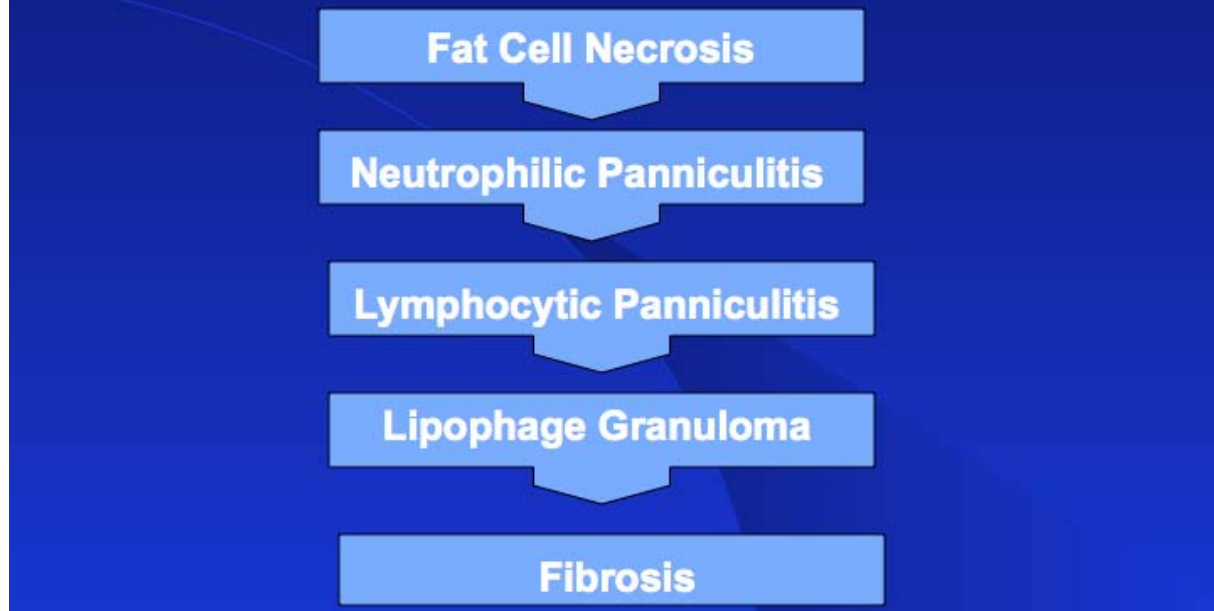


Schematic depiction: Injection lipolysis





## **Mode of Action of Injection Lipolysis of Lipoma according to Histology**



after studies of Ass. Prof. Dr. F.Bechara et al, Ruhruniversity of Bochum