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REPORT

Overlooked & Overworked

Preventive maintenance for your stomach, liver and pancreas

by Karin Granstrom Jordan, MD

A European soy derivative helps protect vital organs from the effects of toxic overload, obesity, alcohol, aspirin and NSAIDs-and helps maintain a youthful cholesterol profile.

The aging process, combined with deleterious lifestyle habits, inflicts tremendous damage on our vital organs. NSAIDs and aspirin are toxic to the gut, while alcohol is toxic to the liver and pancreas. Our poor diets too often stress the organs of digestion and metabolism, while contributing to the buildup of arterial plaques. The modern diet and alcohol consumption can also lead to obesity that further promotes liver pathology and cardiovascular disease. One of the best things you can do for your future health is to support and optimize the function of the vital organs compromised by those interrelated stressors-the stomach, liver, pancreas and cardiovascular system.



PPC Soy derivative

Phosphatidylcholine (the main component of lecithin) is an integral part of cell membranes, essential for their structural and functional integrity. Cell membranes act like gatekeepers, allowing nutrients into the cells but blocking damaging toxins from gaining entrance. A new extract from soybeans called PPC (polyenylphosphatidylcholine) has been shown to enhance cell membrane function throughout the body.

PPC is approved for the treatment of chronic liver diseases in many European countries and is actually listed in the Physician's Desk Reference (PDR) of the United States. An accumulating body of research suggests that PPC's umbrella of protection may extend from the liver to the stomach, pancreas and cardiovascular system. PPC is well absorbed in humans and animals when taken orally. There are no known contraindications, side effects or interactions with other drugs, even with consumption of large quantities of PPC.

It is believed that PPC's protective effect is based on its ability to be incorporated into normal and damaged cell membranes. Animal studies have indicated that PPC, which is a polyunsaturated phosphatidylcholine, becomes incorporated into the membranes of liver cells as a substitute for native saturated phosphatidylcholine molecules (Stoffel W et al 1978). This substitution is shown to result in an increase in membrane fluidity and active transport activity across the membrane. Similarly, PPC is incorporated into blood lipoproteins such as cholesterol, leading to lipid-lowering properties.

Stomach protection

The consumption of non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin in our society is greater than any other drug class because of their relative effectiveness in the treatment of pain and inflammation. Recently published evidence shows that those who take NSAIDs have lower risks of Alzheimer's disease, cardiovascular disease and certain cancers. It appears that some of the common diseases of aging are caused by a chronic inflammatory cascade and that daily NSAID ingestion affords considerable protection against these disorders.

A major concern with NSAID drugs, though, relates to their well-established ability to induce gastrointestinal injury in the forms of erosion, bleeding, ulceration and perforation. Few people realize that GI toxicity from NSAIDs is the most frequent adverse drug event in the U.S., according to some estimates. The facts are alarming (Raskin JB, 1999; Wolfe MM et al., 1999):

- NSAIDs are used regularly by at least 13 million Americans with arthritic conditions, leading to 16,500 NSAID-related deaths annually (similar to the number of deaths from AIDS).
- NSAID use increases the relative risk of serious gastrointestinal events three-to-fourfold, and higher for the elderly.
- 30-60% of chronic NSAID users develop gastroduodenal erosions; 5-30% of chronic users develop ulcers.
- One third of patients over age 60 with bleeding from peptic ulcers are on NSAIDs.
- Two thirds of patients over age 60 with GI perforations are on NSAIDs.
- Over 100,000 people are hospitalized annually in the U.S. for serious GI complications from NSAID use.

- The mortality rate for patients hospitalized for upper GI bleeding from NSAIDs is 5-10%.
- GI toxicity from NSAID use is the 15th most common cause of death in the U.S.
- Advanced age is a primary risk factor for adverse GI events from NSAID use, and the risk increases steadily with age.

This "silent epidemic" appears without symptoms in up to 40% of cases of NSAID-induced erosive gastritis. While 10-20% of NSAID users have indigestion (dyspepsia), this is not a reliable indicator of mucosal injury. Damage to the gastric epithelium begins within minutes of taking an NSAID, and hemorrhages and erosions follow within hours. In most people the gastric mucosa adapts over time, but studies show that 60-100% of patients on NSAIDs for 1 to 2 weeks develop submucosal hemorrhage, superficial erosions, erythema (inflammation of mucous membranes), or blood in the stool. Moreover, NSAID toxicity extends to the small intestine and large bowel, as manifested in silent ulcerations, colitis-like conditions, and aggravation of inflammatory bowel disease.

Doses of aspirin as low as 30 mg suppress the production of protective prostaglandins in the gastric mucosa. In addition, aspirin's direct contact with the gastrointestinal tract interferes with the hydrophobic "non-wettable" properties that protect the underlying epithelium from gastric acid and other toxic substances. This characteristic seems to be attributable to an extracellular lining of phospholipids, which are synthesized in surface mucus cells of the stomach. Aspirin and other NSAIDs can rapidly transform the gastric mucosa from a non-wettable to a wettable state, thereby increasing the tissue's susceptibility to the corrosive actions of gastric acid.

A study on experimentally induced gastric ulcers in rats (Dunjic BS, et al., 1993) showed that mucosal lesions were significantly reduced by a single dose of PPC given before or after the injury factor, which in this study was ethanol or an NSAID.

A recent clinical trial compared the GI effects of aspirin to those of aspirin complexed with PPC (Anand BS et al., 1999). Sixteen healthy subjects were given either ten doses of aspirin or ten doses of the aspirin/PPC complex over a 72 hour period. After a "washout" period, subjects were switched over to the other medication for a 72 hour period.

Researchers counted the number of gastroduodenal erosions in each subject. Those taking aspirin had an average of 8.75 erosions, while those taking the aspirin/PPC complex averaged only 2.81 erosions. The protective effect of PPC was most apparent in those who were most susceptible to aspirin injury, and did not interfere with the therapeutic activity of the aspirin.

(Editors note: The cardio-protective benefits of aspirin are substantial. In addition to reducing abnormal arterial blood clot formation, aspirin suppresses a dangerous pro-inflammatory agent called C-reactive protein. The latest finding about heart attack risk shows that C-reactive protein causes a lethal inflammatory cascade on the inner arterial wall. What happens is that C-reactive protein induces atherosclerotic plaque on the arterial wall to burst open like popcorn, blocking a coronary artery and causing a heart attack. Aspirin specifically suppresses C-reactive protein. Now that PPC supplements are available, taking low-dose aspirin can be made a lot safer for those who take it as a preventive.)

Cholesterol and angina reduction

PPC's beneficial effects on blood lipoproteins have been demonstrated in a series of animal and human studies. A clinical trial conducted in St. Petersburg, Russia, (Klimov AN et al., 1995) compared PPC to niacin in angina patients with a hereditary elevation of cholesterol and triglycerides. Niacin is considered a standard treatment for this condition, but adverse effects are fairly common. These include flushing, skin dryness and itching, GI disturbances, elevation of liver enzymes, decline in glucose tolerance, and reduced urinary excretion of uric acid.

In this study, 100 patients were randomly assigned to receive either PPC or niacin for six months. Patients in both groups were put on a low-fat cholesterol free diet, and any lipid-lowering medications they had been taking were discontinued four weeks before the start of the trial. For the first two weeks of the trial, PPC was given intravenously (500 mg/day); for the remaining five and a half months, patients took 600 mg of PPC in capsules three times a day.

Both medications reduced the frequency of angina attacks, from 2.3 per week to 0.9 in the niacin group, and from 3.8 to 0.9 in the PPC group. Eight patients (16%) in the niacin group dropped out due to adverse effects of the medication, while the patients in the PPC group were entirely free of side effects. Only the PPC group showed a significant improvement in exercise tolerance. PPC significantly reduced oxidation of apoB lipoprotein, while niacin did not. The two medications improved the overall lipoprotein profile of the patients to a similar extent. PPC lowered total and LDL cholesterol by about 15%, and triglycerides by 32%.

PPC also raised levels of the "good" HDL cholesterol by 10%. It is fortunate that the researchers looked beneath the surface of this modest increase, where they discovered a fascinating phenomenon.

HDL and longevity

It is well known that the most protective subfraction of HDL cholesterol is the one with the largest particles, known as HDL2b. When rhesus monkeys are placed on a calorie restricted diet to slow the aging process, their HDL2b levels increase significantly (Verdery RB et al., 1997). A study of centenarian women provided dramatic evidence of the cardioprotective importance of this subfraction (Barbagallo CM et al., 1998). Lipoprotein profiles of the centenarians were compared to those of healthy middle-aged and elderly women of the same weight. There were no significant differences found between the centenarians and the younger women in the battery of tests, which included plasma lipids, apolipoprotein, and Lp(a)-except in HDL2b and HDL3a levels. While the total HDL

levels were about the same, HDL2b levels were significantly increased in the centenarians, and HDL3a levels were significantly decreased, compared to the other groups. The researchers call for further study of the distribution of HDL subfractions as a possible marker of longevity.

Such a major shift in the distribution of HDL subfractions—from HDL3a to HDL2b—also occurred in the PPC group of the Russian study, but not in the niacin group. Thus, while total HDL levels rose modestly after PPC supplementation, the desirable HDL2b subfraction rose preferentially due to a shift from the 2a and 3a subfractions to the highly antiatherogenic 2b subfraction. Thus PPC may exert an anti-aging effect on the cardiovascular system, a prospect meriting further research.

High serum lipids are common in diabetic patients (approx. in 50%), and the incidence of coronary heart disease is high. In a double-blind study on the lipoprotein profile in diabetic patients (Kirsten R et al., 1994), 30 non-insulin-dependent diabetics with secondary hyperlipidemia received 2.7 g PPC or placebo daily over a 2-month period. LDL-cholesterol and triglyceride levels decreased significantly when compared with the placebo group, and HDL cholesterol levels increased (see table). In the control group the values did not change throughout the trial.

Moderate alcohol intake has been shown to improve the lipoprotein profile, and especially to raise HDL cholesterol levels. A study on rats shows that PPC preserves the HDL elevating effect of alcohol, while decreasing LDL and VLDL cholesterol levels after eating (Navder KP et al., 1997).

However, higher levels of alcohol consumption are toxic to the liver, and increase oxidation of LDL cholesterol. New research on baboons shows that PPC markedly reduces alcohol-induced oxidation of LDL, thus helping to protect against one of the mechanisms that promotes atherosclerosis in heavy drinkers (Navder KP et al., 1999). At the same time, PPC helps protect the liver from alcohol toxicity.

Fatty liver

The liver is the largest organ of the body, responsible for metabolizing the food we eat (breaking it down into useful parts) and protecting us from the damaging effects of the numerous toxic compounds that we are exposed to on a daily basis. But what protects the liver so that it can in turn protect the rest of the body? The liver is unfortunately susceptible to toxicity itself, and to an insidious condition called steatosis thought to be a precursor to many serious liver diseases. Steatosis, also called fatty liver, is a common finding in human liver biopsies. It is a condition in which fat has accumulated within liver cells (hepatocytes) without causing any specific symptoms. As we shall discuss, PPC may help correct steatosis.

Fatty liver as a longstanding chronic condition can occur in association with a wide range of diseases, toxins and drugs, although in clinical practice, the majority of cases are due to alcohol excess, diabetes and obesity. Much less common are occurrences of acute fatty liver during pregnancy and as a response to administration of tetracyclines, acetaminophen and other drugs and toxins.

Fatty liver had long been believed to be a benign reversible condition. Careful clinical studies, however, demonstrate that fatty liver of either alcoholic or non-alcoholic origin can lead to inflammation, cell death and fibrosis (steatohepatitis), and eventually even cirrhosis. Cirrhosis is the irreversible end result of fibrous scarring, a response of the liver to a variety of long-standing inflammatory, toxic, metabolic and congestive damage.

Alcohol is by far the commonest cause both of steatosis and cirrhosis in the Western world. However, there is a considerable inter-individual difference in the degree of liver damage produced by excessive alcohol intake. There seem to be no clear correlations between the incidence and severity of fatty liver and either the amount, type or duration of alcohol abuse. It has been unclear why in some individuals steatosis, whatever its etiology, never progresses to steatohepatitis and cirrhosis.

A growing body of evidence suggests that the oxidation of fat in the liver leads to the development of liver damage, and free radicals have been demonstrated to play an important role in the hepatotoxic effect of many substances. The oxidation of fats takes place through a chain reaction called lipid peroxidation that impairs the anatomical and functional integrity of membranes and creates new toxic substances that further extend the damage. PPC's antioxidant action may help explain its effectiveness in treating fatty liver, as demonstrated by a study carried out in the Czech Republic (Horejsova M and Urban J, 1994).

This Czech study of 28 women with steatosis of various origins showed PPC to be a highly effective therapy for fatty liver. The women were given PPC along with unsaturated fatty acids and low-dose B vitamins and vitamin E. After six months, ultrasound examinations revealed that eight of the women were free of apparent steatosis, 13 had improved, while the remaining seven showed no change. Abnormal enlargement of the liver (hepatomegaly) was significantly reduced, and the working tissue of the liver (parenchyma) became homogeneous in 10 of the 11 cases where it had been abnormal.

Lab tests showed highly significant declines in all of the liver enzyme levels measured (ALT, AST, GMT). There were also significant declines in bilirubin, cholesterol and triglycerides. Overall, 54% of the patients in the study improved in all parameters studied, as determined by ultrasound assessment, lab tests and subjective evaluation. Forty-three percent showed improvement in lab tests and subjective evaluation, and only 3.6% did not show any objective improvement.

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Hepatopro (formerly GastroPro) a phosphatidylcholine product, is available from Life Extension.

[Back to the Magazine Forum](#)

REPORT

Continued from
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Fibrosis, cirrhosis and alcohol

A characteristic feature of liver disease, regardless of its cause, is the increased deposition of collagen, the connective tissue protein. This increased collagen accumulation could result from enhanced collagen biosynthesis and/or decreased collagen breakdown. PPC appears to increase collagen breakdown by stimulating collagenase activity in hepatic stellate cells preventing the development of fibrosis and cirrhosis (Li J et al., 1992). Several studies have focused on PPC and its effect on collagen and fibrosis.

A baboon study (Lieber CS et al., 1994) confirmed earlier results (Lieber CS et al., 1990) showing that in the baboon, feeding of ethanol (a form of alcohol) results in hepatic fibrosis and cirrhosis even when associated with an adequate diet. This effect could be prevented by supplementing the diet with a 94-96% pure PPC preparation. None of the eight animals fed alcohol with PPC for up to 6.5 years had progression to fibrosis or cirrhosis as had 10 of 12 unsupplemented baboons, a highly significant difference. Another study (Ma X et al., 1996) revealed that PPC reduces hepatic fibrosis induced by either carbon tetrachloride or human albumin in rats, and that PPC not only prevents the development of fibrosis but accelerates the regression of pre-existing fibrosis. The study further suggested that the protective effect exerted by PPC against fibrosis is due, at least in part to increased collagen breakdown.

One of the ways PPC helps prevent liver damage from alcohol is by inhibiting an enzyme known as CYP 2E1. Chronic alcohol consumption raises levels of this enzyme, which is involved in the metabolism of alcohol. This leads to oxidative stress and acetaldehyde production, which stresses the antioxidant defense system and depletes glutathione. CYP 2E1 also furthers the production of toxic metabolites from common drugs such as acetaminophen and promotes carcinogenesis. CYP 2E1 inhibitors protect the liver from alcohol-induced damage, but drugs tested for this purpose have been too toxic for practical use. However it has recently been discovered that PPC significantly inhibits CYP 2E1 activity (Lieber CS, 1999; Aleynik MK et al., 1999), providing a potential nontoxic solution to this problem.

Antioxidant effects

As we have seen, a key mechanism of PPC action is its antioxidant effect. Despite its rich content of polyunsaturated linoleic acid, PPC has been shown to effectively reduce oxidative stress caused by alcohol in the liver and pancreas, as well as in LDL cholesterol.

Newly published research (Aleynik SI, Leo MA, Takeshige U et al., 1999) identifies the constituent of PPC primarily responsible for its antioxidant effect. This constituent, DLPC, comprises 40-52% of PPC. The researchers found that the "remarkable" antioxidant effect of PPC on oxidative stress induced in hepatoma cells by arachidonic acid could be accounted for by the DLPC contained in it.

DLPC appears to be primarily responsible for many of the protective actions of PPC on the liver and pancreas. A new study demonstrates that DLPC stimulates the Kupffer cells of the liver to decrease production of the hepatotoxic tumor necrosis factor- α , while increasing production of the hepatoprotective interleukin-1b (Oneta CM et al., 1999). DLPC also appears to decrease activation of collagen-producing stellate cells in the liver, and to increase collagenase activity and thus collagen breakdown, as discussed above.

The benefits of protection

Modern living unfortunately involves daily exposure to substances that are toxic to our bodies, which can impose heavy stresses on the vital organs we have discussed. Therefore it is logical to think that all of us can benefit from some kind of support in maintaining the vitality of these organs. In particular, individuals with a substantial alcohol consumption, with obesity, diabetes or with high exposure to NSAIDs or environmental toxins have an even greater reason to take protective measures because of the documented risk of developing serious pathologies.

Knowing that conventional medicine has very little to offer in the prevention or early treatment of the disorders we have discussed, it seems wise to remember that prevention is the best cure. We are fortunate today to have access to a natural protective remedy that is safe, effective and without significant side effects.

And it is good to know that protection of the liver, pancreas and stomach is beneficial not only for these vital organs themselves, but for the overall health and vitality of our body.

Obesity and Steatohepatitis

Among the causes for non-alcoholic steatohepatitis (NASH), obesity is considered to be the most common. There is evidence to suggest that liver disease actually can be considered a complication of obesity. No major prospective longitudinal studies of NASH have been carried out. It seems, however, that the risk of progression to cirrhosis is generally low for non-obese individuals but significant among obese individuals. There is no predictable correlation between symptoms (or lack of them), abnormality of liver function tests and severity of liver tissue damage.

In a study of 50 unselected, obese (21-130% above ideal body weight) subjects admitted to the hospital for weight reduction, Braillon et al (1985) found that 10% had normal livers, 48% fatty livers, 26% steatohepatitis, 8% fibrosis and 8% cirrhosis.

Interestingly, it has been observed among patients with fatty liver related to obesity, that rapid weight loss caused by dieting and intestinal bypass surgery increase the risk for developing steatohepatitis. The resulting increase in the concentration of fatty acids and/or ketones within the liver severely augments the generation of free radicals (Day CP et al.: 1994).

A study by Yang et al (1997) indicates that obesity also increases susceptibility to endotoxin-mediated liver injury. Endotoxins are cell wall components produced by intestinal gram-negative bacteria, thought to play a role in liver injury induced by alcohol and other hepatotoxins. Under normal conditions they are absorbed into the portal venous circulation and detoxified in the liver. Hepatic dysfunction will interfere with this clearing mechanism and amplify the negative activities of endotoxin, such as lipid peroxidation, reduced detoxification by the cytochrome P-450 enzymes, and impairment of the immune system.

Berson et al., 1998 summarizes the insights from the new research on the mechanisms of steatohepatitis well: Its development requires a double hit, the first producing steatosis, the second a source of oxidative stress capable of initiating significant lipid peroxidation. This concept provides a rationale for both the treatment and prevention of disease progression in steatosis of alcoholic and non-alcoholic causes. Management strategies should ideally be directed at reducing the severity of steatosis and at avoiding and removing the triggers of inflammation and fibrosis. Specific treatment modalities for at-risk individuals might include sensible weight reduction, cessation of exposure to toxins and treatment with antioxidants and inhibitors of peroxisomal β -oxidation.

PPC in hepatitis

PPC has been found to decrease serum aminotransferases in experimental hepatitis. In 1998, Niederau et al. conducted a multi-center randomized, placebo-controlled clinical study evaluating the effects of PPC in combination with interferon alpha (IFN) in patients suffering from Hepatitis B and C. IFN is the standard treatment for these diseases, however only 50% of patients with Hepatitis B and 20-30% of patients with Hepatitis C respond to this antiviral drug with long-term normalization of serum aminotransferases. Among patients with hepatitis C that do respond to IFN while under treatment, there is at least a 50% relapse rate. Evidently there is a need for more effective treatment.

In this study 176 patients completed the protocol. All patients were given the same amount of interferon during the 24-week test period. In addition patients were randomly assigned to receive either 1.8 grams per day of PPC or placebo for the same 24 weeks. A biochemical response to therapy was defined as minimum 50% reduction of ALT compared to pre-treatment values.

The results show that PPC increased the response rate to IFN in chronic viral hepatitis C (71% versus 51 % in the placebo group). Prolonged PPC therapy given to responders 24 weeks beyond the cessation of interferon therapy tended to increase the rate of sustained responses in patients with hepatitis C (41% versus 15%). Hepatitis B patients, however, did not have an improved biochemical response to interferon from PPC. The reason why PPC showed beneficial effect in hepatitis C and not in hepatitis B is not clear and will be further investigated.

This study suggests that PPC can be a valuable adjunct to IFN treatment of Hepatitis C as well as be of beneficial use after cessation of IFN therapy in order to increase the chance of sustained response to therapy.

Alcohol and the pancreas

The pancreas is essential to both digestion and glucose regulation. It secretes digestive enzymes into the duodenum for protein, carbohydrate and fat digestion, and produces large amounts of sodium bicarbonate (as found in baking soda) to neutralize stomach acid in the duodenum. The islets of the pancreas produce insulin and the related hormones glucagon and somatostatin.

Pancreatitis-inflammation of the pancreas-is caused primarily by overconsumption of alcohol in about 80% of cases. Ethanol causes severe oxidative stress in the pancreas, probably due to increased production of free radicals and depletion of glutathione and other antioxidants. In particular, both alcohol intake and pancreatitis are associated with rises in the CYP 2E1 enzyme in the pancreas.

The research group that investigated the correction of alcohol-induced liver damage by PPC has recently published research demonstrating the same protective effect in the pancreas (Aleynik SI, Leo MA, Aleynik MK et al., 1999). When rats were given ethanol, markers of oxidative stress in the pancreas rose sharply. However PPC given along with the ethanol prevented this rise, and almost completely alleviated the depletion of pancreatic glutathione caused by ethanol.

The protective effect of PPC on oxidative stress in the pancreas was even more pronounced than these researchers had observed in the liver of baboons fed alcohol. PPC may protect the pancreas from other causes of oxidative stress; as the authors state, PPC "could provide innocuous but effective and orally active antioxidant therapy, not only as shown before for liver injury, but also, as shown here, for early pancreatic changes."

Gastropro, a phosphatidylcholine product, is available from Life Extension

References

- Aleynik MK et al.: Polyenylphosphatidylcholine opposes the increase of cytochrome P-4502E1 by ethanol and corrects its iron-induced decrease. *Alcohol Clin Exp Res* 23(1):96-100, 1999
- Aleynik SI, Leo MA, Aleynik MK et al.: Alcohol-induced pancreatic oxidative stress: Protection by phospholipid repletion. *Free Radic Biol Med* 26 (5/6): 609-619, 1999
- Aleynik SI, Leo MA, Takeshige U et al.: Dilinoleoylphosphatidylcholine is the active antioxidant of polyenylphosphatidylcholine. *J Investig Med* 47(9):507-12, 1999
- Anand BS et al.: Phospholipid association reduces the gastric mucosal toxicity of aspirin in human subjects. *Am J Gastroenterol* 94(7):1818-22, 1999
- Barbagallo CM et al.: Lipoprotein profile and high-density lipoproteins: subfractions distribution in centenarians. *Gerontology* 44 (2):106-10, 1998
- Berson A et al.: Steatohepatitis-inducing drugs cause mitochondrial dysfunction and lipid peroxidation in rat hepatocytes. *Gastroenterology* 114(4):764-74, 1998
- Biagi PL et al.: The effect of dietary polyenylphosphatidylcholine on microsomal delta-6-desaturase activity, fatty acid composition, and microviscosity in rat liver under oxidative stress. *J Nutr Biochem* 4: 690-94, 1993
- Braillon A et al.: Liver in obesity. *Gut* 26(2): 133-39, 1985
- Day CP et al.: The biochemistry of alcohol-induced fatty liver. *Biochim Biophys Acta* 1215: 33-48, 1994
- Dunjic BS et al.: Gastroprotective capability of exogenous phosphatidylcholine in experimentally induced chronic ulcers in rats. *Scand J Gastroenterol*; 28: 89-94, 1993
- Fabia R et al.: Effects of phosphatidylcholine on acetic acid-induced colitis in the rat. *Digestion* 53: 35-44, 1992
- Galli C et al.: Oral polyunsaturated phosphatidylcholine reduces platelet lipid and cholesterol contents in healthy volunteers. *Lipids* 20(9):561-6, 1985
- Holecek M et al.: Effect of polyunsaturated phosphatidylcholine on liver regeneration onset after hepatectomy in the rat. *Arzneimittelforschung* 42(3): 337-39, 1992
- Horejsova M and Urban J: The effect of polyene phosphatidylcholine (Essentiale forte) in the treatment of liver steatosis and ultrasound findings--preliminary study. *Cas Lek Cesk* 133(12):366-9, 1994
- James OFW et al.: Non-alcoholic steatohepatitis (NASH): a disease of emerging identity and importance. *J Hepatol* 29: 495-501, 1998
- Kesaniemi YA et al.: Effects of dietary polyenylphosphatidylcholine on metabolism of cholesterol and triglycerides in hypertriglyceridemic patients. *Am J Clin Nutr* 43: 98-107, 1986
- Kirsten R et al.: Polyenylphosphatidylcholine improves the lipoprotein profile in diabetic patients. *Int J Clin Pharmacol Ther* 32(2): 53-6, 1994
- Klimov AN et al.: "Essential" phospholipids versus nicotinic acid in the treatment of patients with type IIB hyperlipoproteinemia and ischemic heart disease. *Cardiovasc Drugs Ther* 9(6):779-84, 1995
- Li J et al.: Polyunsaturated lecithin prevents acetaldehyde-mediated hepatic collagen accumulation by stimulating collagenase activity in cultured lipocytes. *Hepatology* 15(3): 373-381, 1992
- Lichtenberger LM et al.: Non-steroidal anti-inflammatory drugs (NSAIDs) associate with zwitterionic phospholipids: Insight into the mechanism and reversal of NSAID-induced gastrointestinal injury. *Nature Medicine* 1(2): 154-58, 1995
- Lieber CS et al.: Attenuation of alcohol-induced hepatic fibrosis by polyunsaturated lecithin. *Hepatology* 12(6): 1390-98, 1990
- Lieber CS et al.: Phosphatidylcholine protects against fibrosis and cirrhosis in the baboon. *Gastroenterology* 106: 152-159, 1994

Lieber CS: Microsomal ethanol-oxidizing system (MEOS): the first 30 years (1968-1998)--a review. Alcohol Clin Exp Res 23(6):991-1007, 1999

Ma X et al.: Polyenylphosphatidylcholine attenuates non-alcoholic hepatic fibrosis and accelerates its regression. J Hepatol 24: 604-613, 1996

Navder KP et al.: Polyenylphosphatidylcholine decreases alcoholic hyperlipemia without affecting the alcohol-induced rise of HDL-cholesterol. Life Sci 61(19): 1907-14, 1997

Navder KP et al.: Oxidation of LDL in baboons is increased by alcohol and attenuated by polyenylphosphatidylcholine. J Lipid Res 40(6):983-7, 1999

Niederau C et al.: Polyunsaturated phosphatidylcholine and interferon alpha for treatment of chronic hepatitis B and C: A multi-center, randomized, double-blind, placebo-controlled trial. Hepatogastroenterology 45: 797-804, 1998

Oneta CM et al.: Dilinoleoylphosphatidylcholine selectively modulates lipopolysaccharide-induced Kupffer cell activation. J Lab Clin Med 134(5):466-70, 1999

Raskin JB: Gastrointestinal effects of nonsteroidal anti-inflammatory therapy. Am J Med 106(5B), 1999

Stoffel W et al.: Pleomorphic functions of highly unsaturated phospholipids in biological membranes and serum lipoproteins. Med Welt 29(4): 124-31, 1978

Verdery RB et al.: Caloric restriction increases HDL2 levels in rhesus monkeys (*Macaca mulatta*). Am J Physiol 273(4 Pt 1):E714-9, 1997

Wallace LA et al.: Personal exposures, indoor-outdoor relationships and breath levels of toxic air pollutants measured for 355 persons in New Jersey. EPA 0589, 1989

Wang XD, Andersson R et al.: Phospholipids prevent enteric bacterial translocation in the early stage of experimental acute liver failure in the rat. Scand J Gastroenterol 29:1117-21, 1994

Weltman MD et al.: Hepatic cytochrome P450 2E1 is increased in patients with nonalcoholic steatohepatitis. Hepatology 27(1): 128-133, 1998

Wolfe MM et al.: Gastrointestinal toxicity of nonsteroidal anti-inflammatory drugs. NEJM 340(24):1888-99, 1999

Yamada S et al.: Chronic ethanol consumption alters rat liver plasma membranes and potentiates release of alkaline phosphatase. Gastroenterology 88(6): 1799-806, 1985

Yang SQ et al.: Obesity increases sensitivity to endotoxin liver injury: Implications for the pathogenesis of steatohepatitis. Proc Natl Acad Sci USA 94: 2557-62, 1997

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