

LE Magazine June 2000

ABSTRACTS

FEATURED:

Rebuttals

Vitamin C

Silibinin/Silymarin

Rebuttals

Reprint rebuttals to the American Heart Association's attack on vitamin C from the Linus Pauling Institute, The Vitamin C Foundation and Dr. Robert Cathcart.

Rebuttal from the Linus Pauling Institute

Study links vitamin C pills with faster clogging of the arteries? Another unconfirmed study causing unnecessary confusion and fear among the public.

A study reported on March 2, 2000, by Dr. James Dwyer at an American Heart Association meeting in San Diego allegedly raised the possibility that taking vitamin C supplements may speed up clogging of the arteries, or atherosclerosis. Although the researchers themselves called their findings "a surprise" and cautioned that more experiments are needed to investigate whether vitamin C supplements may be harmful, the study was released to the media without discussing its limitations nor putting it in the proper context of the hundreds of existing studies demonstrating the health benefits of vitamin C. Both the researchers and the American Heart Association acted irresponsibly by releasing this unconfirmed study without appropriate background information, causing unnecessary confusion and fear among the public.

Dr. Dwyer reported that subjects taking 500 milligrams of vitamin C daily for at least a year had a 2.5 times greater rate of thickening of the carotid artery wall than did subjects who did not take supplements. These results are in direct conflict with a study published in 1995 in the American Heart Association journal *Circulation*, which found a significant reduction in carotid artery wall thickness in people over 55 years old who consumed amounts of vitamin C greater than 982 mg per day compared to those consuming less than 88 mg per day.

If the results by Dwyer and colleagues were true, people who take vitamin C supplements should die of heart attacks and strokes at a much greater rate than non-supplement users. However, there is no scientific evidence in support of this notion. Many epidemiological studies and some clinical trials have indicated that dietary intake of or supplementation with vitamin C is associated with a reduction in the incidence of chronic disease morbidity and mortality, including cardiovascular diseases. Numerous epidemiological studies have shown a significantly decreased heart attack or stroke risk with increased vitamin C intake.

A large epidemiological study published in 1992 showed a risk reduction for heart disease of 45% in men and 25% in women consuming greater than 50 mg of vitamin C daily from the diet plus regular supplements, corresponding to a total vitamin C intake of about 300 mg per day. Although this study indicated that vitamin C supplements provide cardiovascular benefits above and beyond the vitamin C obtained from the diet, two other large epidemiological studies published in 1996 found no effect on heart disease risk in people who take regular vitamin C supplements. However, not a single epidemiological study nor clinical trial has found an increased risk of heart attacks or strokes in people taking vitamin C supplements.

Over twenty clinical studies since 1996 published primarily in *Circulation* have consistently found beneficial effects of vitamin C, administered either orally or by intra-arterial infusion, on the relaxation of arteries, or vasodilation. Impaired vasodilation is an important risk factor for heart attacks and strokes.

Vasodilation in patients with heart disease is significantly improved following supplementation with 500 mg of vitamin C per day for 30 days, and is comparable to vasodilation seen in healthy people. Beneficial effects of vitamin C supplements leading to normalization of vasodilation were also observed in patients with angina, heart failure, high cholesterol levels, hypertension, diabetes, high homocysteine levels and in smokers. In addition, a recent study in *Lancet* has demonstrated that 500 mg of vitamin C per day given for 30 days lowers blood pressure in moderately hypertensive patients. High blood pressure is a major risk factor for heart disease.

Several limitations of the study reported by Dwyer and colleagues need to be pointed out. First, this was an oral presentation of an abstract, meaning that the study has not been published in the scientific literature after undergoing rigorous peer review. The measurement of carotid artery wall thickness by ultrasound poses significant technical problems and is notoriously difficult.

The differences observed are exceedingly small, and control measurements and strict blinding of the researchers evaluating the data are pivotal. Second, because this is an epidemiological study, the observed associations between vitamin C intake and carotid atherosclerosis do not prove cause-effect relationships, and may reflect differences in diet or lifestyle. There also can be significant confounding by unmeasured risk factors or imperfect statistical adjustments of the data. The vitamin C intakes were estimated, but no actual measurements of vitamin C in the blood of the subjects were made. Third, it is known that in healthy people cells and tissues are saturated at an intake of 100 to 200 mg of vitamin C per day. Therefore, it is difficult to rationalize any effects of vitamin C above these intake levels, as tissue levels would not be altered.

People taking vitamin C supplements should continue to do so, as the known health benefits of vitamin C far outweigh alleged,

unconfirmed risks. There is no scientific evidence that vitamin C supplements increase the risk of heart attacks or strokes. Vitamin C supplements of 500 mg per day have been shown to normalize vasodilation and lower blood pressure, two major cardiovascular risk factors.

LRebuttal to the American Heart Association report by Dr. Cathcart:

The recent story linking vitamin C "pills" with "clogging" of the arteries.

We have been in contact with Professor James Dwyer of the USC Medical School, one of the principal researchers. As expected, this research seems to be good news for elderly vitamin C takers whose carotid arteries have "thinned" with age. There is no evidence of occlusion (or clogging), contrary to the media reports.

Here is what we have confirmed with Dr. Dwyer:

- There is no paper as we suspected. (The USC team's paper is in "peer review" and not available.)
- The USC team used a new "B-mode" imaging technique which is still undergoing clinical trial for accuracy at the NIH.
- This B-mode imaging technique has three indicators. The USC team only studied one; carotid arterial "thickening" or "IMT." (Dr. Dwyer tells us there will be no reference in their paper to the other two occlusion indicators; plaque index and velocity ratio.)
- According to correspondence, Dr. Dwyer and the USC team is unaware that arteries might get thicker with increased vitamin C intake, and that this is entirely predicted by theory. (Increased vitamin C stimulates collagen production, but this is not well taught or well known in medical school.)
- Last year, the same USC research team (Dwyers, et. al) wrote a paper with the opposite findings. Last year they found that stress (some would say a vitamin C deficiency) leads to early atherosclerosis in men (March 1999).

Bottom line: There is no evidence of occlusion, only thickening. Now we need your help repairing the damage caused by the premature release of this unpublished research. Millions of people are now afraid of vitamin C. Please help spread the word. We will post more information as it becomes available at: <http://www.vitaminfoundation.org/>.

My experience with 25,000 patients since 1969 indicates that this charge is ridiculous. I know that follow-up is not perfect in private practice but I have had no patient who had a good heart when I first saw them and who took massive doses of C who ever developed heart problems. I have to add that I advise all my patients to avoid sugar, chemicals and highly process foods, and put them on a number of other nutrients. If it turns out that there is thickening of the carotid, I think it is reversing the thinning that occurs with aging. It is interesting that the effect is so dramatic in the reversing of the effect on smokers. I have to congratulate you at the Vitamin C Foundation on unveiling the other two findings that could have been measured which were not reported.

Probably the finding that C helped would not be publishable.

Dr. Cathcart is a leading expert on treating people with high doses of vitamin C. Visit his website at orthomed.com.

Rebuttal by The Vitamin C Foundation

Here is some technical information on the B-mode imaging process. Note there are three measures, yet the USC paper will only mention one. The missing two measures are used to infer occlusion.

Detailed B-mode images of the right and left common carotid artery, common carotid bifurcation, and the first centimeter of the internal carotid artery are obtained. Selected images are digitized for later measurement of intima-media thickness. After imaging, the sonographer obtains pulsed wave Doppler measures of blood flow velocity at the mid common (2 cm proximal to the carotid bulb) and in the internal carotid artery at the point of highest velocity distal to the flow divider. These are used to calculate the degree to which plaque may be interfering with blood flow.

The scanning and reading protocols result in three primary carotid disease measures:

- Average wall intima-media thickness
- A measure of degree of focal plaque called the plaque index
- The velocity ratio, a determination of whether or not plaque is interfering with blood flow in the internal carotid artery

Again, the USC team's report will only concern arterial thickness. The occlusion indicators are not reported for reasons unknown.

Owen R. Fonorow
The Vitamin C Foundation
<http://www.vitaminfoundation.org/>

Vitamin C

On the role of vitamin C and other antioxidants in atherogenesis and vascular dysfunction

Oxidative stress has been implicated as an important etiologic factor in atherosclerosis and vascular dysfunction. Antioxidants may inhibit atherogenesis and improve vascular function by two different mechanisms. First, lipid-soluble antioxidants present in low-density lipoprotein (LDL), including alpha-tocopherol, and water-soluble antioxidants present in the extracellular fluid of the arterial wall, including ascorbic acid (vitamin C), inhibit LDL oxidation through an LDL-specific antioxidant action. Second, antioxidants present in the cells of the vascular wall decrease cellular production and release of reactive oxygen species (ROS), inhibit endothelial activation (i.e., expression of adhesion molecules and monocyte chemoattractants), and improve the biologic activity of endothelium-derived nitric oxide (EDNO) through a cell- or tissue-specific antioxidant action. alpha-Tocopherol and a number of thiol antioxidants have been shown to decrease adhesion molecule expression and monocyte-endothelial interactions. Vitamin C has been demonstrated to potentiate EDNO activity and normalize vascular function in patients with coronary artery disease and associated risk factors, including hypercholesterolemia, hyperhomocysteinemia, hypertension, diabetes, and smoking.

Proc Soc Exp Biol Med 1999 Dec;222(3):196-204

Vitamin C prevents the acute atherogenic effects of passive smoking

During passive smoking the body is attacked by an excess of free radicals inducing oxidative stress. In nonsmoking subjects even a short period of passive smoking breaks down serum antioxidant defense (TRAP) and accelerates lipid peroxidation leading to accumulation of their low-density lipoprotein (LDL) cholesterol in cultured human macrophages. We now studied whether these acute proatherogenic effects of secondhand smoke could be prevented by an effective free radical scavenger, vitamin C. Blood samples were collected from nonsmoking subjects ($n = 10$) as they were consecutively exposed to normal air or cigarette smoke during four separate days. During the last 2 d, a single dose of vitamin C (3 g) was given, which doubled its plasma concentration. Vitamin C did not influence the plasma antioxidant defense or the resistance of LDL to oxidation in normal air, but prevented the smoke-induced decrease in plasma TRAP ($p < .001$), the decrease in the resistance of LDL to oxidation ($p < .05$), and the accelerated formation of serum thiobarbituric acid reactive substances (TBARS) ($p < .05$) otherwise observed 1.5 h after the beginning of passive smoking. Vitamin C protected nonsmoking subjects against the harmful effects of free radicals during exposure to secondhand smoke.

Free Radic Biol Med 2000 Feb 1;28(3):428-36

Vitamin C and cardiovascular disease: a systematic review

BACKGROUND: Laboratory studies suggest that antioxidants, such as Vitamin C, are important inhibitors of atherosclerotic lesions. Most epidemiological reviews have considered all antioxidants together. This review seeks to clarify the current state of knowledge specifically concerned with vitamin C. **METHODS:** All ecological studies, case-control studies, prospective studies and trials in humans that examined the association between vitamin C intake or blood levels of vitamin C and cardiovascular disease were included. Relevant references were located by MEDLINE search for articles published from 1966 to 1996, by an EMBASE search for articles published from 1980 to 1996, by searching personal bibliographies, books and reviews and from citations in located articles. **RESULTS:** For coronary heart disease four of seven ecological studies, one of four case-control studies and three of 12 cohort studies found a significant protective association with vitamin C intake or status. For strokes two of two ecological studies, none of one case-control study and two of seven cohort studies found a significant protective association. For total circulatory disease, two of three cohort studies reported a significant protective association. **CONCLUSIONS:** The evidence, albeit limited, is consistent with vitamin C having protective effect against stroke whereas the evidence that vitamin C is protective against coronary heart disease is less consistent. The lack of an association for coronary heart disease could be explained in terms of there being a true lack of effect, dietary measurement error, a threshold effect, and effect of seasonal variations in intake, an interaction with other dietary constituents or a relatively short duration of follow-up.

J Cardiovasc Risk 1996 DEC;3(6):513-21

Oral vitamin C reduces arterial stiffness and platelet aggregation in humans

Atherosclerosis is associated with stiffening of conduit arteries and increased platelet activation, partly as a result of reduced bioavailability of nitric oxide (NO), a mediator that normally has a variety of protective effects on blood vessels and platelets. Increased levels of oxygen free radicals are a feature of atherosclerosis that contributes to reduced NO bioavailability and might lead to increased arterial stiffness and platelet activation. Vitamin C is a dietary antioxidant that inactivates oxygen free radicals. This placebo-controlled, double-blind, randomized study was designed to establish whether acute oral administration of vitamin C (2 g), would reduce arterial stiffness and in vitro platelet aggregation in healthy male volunteers. Plasma vitamin C concentrations increased from 42 ± 8 to 104 ± 8 μM at 6 h after oral administration, and were associated with a significant reduction in augmentation index, a measure of arterial stiffness (by $9.6 \pm 3.0\%$; $p = 0.016$), and ADP-induced platelet aggregation (by $35 \pm 13\%$; $p = 0.046$). There was no change in these parameters after placebo. Vitamin C, therefore, appears to have beneficial effects, even in healthy subjects. The mechanism responsible is likely to involve protection of NO from inactivation by oxygen free radicals, but this requires confirmation. If similar effects are observed in patients with atherosclerosis or risk factors, vitamin C supplementation might prove an effective therapy in cardiovascular disease.

J Cardiovasc Pharmacol 1999 Nov;34(5):690-3

Vitamin C improves endothelial function of epicardial coronary arteries in patients with hypercholesterolaemia or essential hypertension assessed by cold pressor testing

AIMS: There is evidence that formation of free radicals increases in patients with hypertension or hypercholesterolaemia, which may contribute to endothelial dysfunction of epicardial coronary arteries due to inactivation of the vasodilator NO. The present study was designed to test whether the abnormal constriction of epicardial coronary arteries due to sympathetic stimulation by the cold pressor test in patients with essential hypertension or hypercholesterolaemia could be reversed by administration of the antioxidant vitamin C. **METHODS and RESULTS:** In 28 patients without relevant coronary artery stenosis the cold pressor test was performed before and after a 3 g infusion of vitamin C. In five normal controls the cold pressor test led to a similar increase in luminal area before and after vitamin C ($3.7\pm 1.3\%$ and $1.9\pm 0.8\%$, ns vs before vitamin C). In nine hypercholesterolaemic patients the cold pressor test led to a $-14.1\pm 2.8\%$ reduction in cross-sectional area before vitamin C. This constriction was significantly improved after vitamin C to -7.6 ± 2.0 , $P=0.027$ vs before vitamin C. In nine hypertensive patients, the cold pressor test led to a $-17.1\pm 3.2\%$ decrease in cross-sectional area before vitamin C, which was improved to -7.1 ± 3.1 after vitamin C, $P=0.004$ vs before vitamin C. This increase in luminal area was significant in each group in comparison with normal controls (each $P<0.05$). Administration of saline (placebo group, five patients) had no significant effect on cold pressor test-induced constriction ($-6.9\pm 3.9\%$ before and $-6.8\pm 3.7\%$ after saline). **CONCLUSION:** The antioxidant vitamin C reverses cold pressor test-induced vasoconstriction of epicardial coronary arteries in patients with hypertension or hypercholesterolaemia. Our data suggest that enhanced oxidative stress contributes to impaired endothelial function in this patient population.

The effectiveness of vitamin C in preventing and relieving the symptoms of virus-induced respiratory infections

BACKGROUND: An ever increasing demand to evaluate the effect of dietary supplements on specific health conditions by use of a "significant scientific" standard has prompted the publication of this study. **OBJECTIVE:** To study the effect of megadose Vitamin C in preventing and relieving cold and flu symptoms in a test group compared with a control group. **DESIGN:** Prospective, controlled study of students in a technical training facility. **SUBJECTS:** A total of 463 students ranging in age from 18 to 32 years made up the control group. A total of 252 students ranging in age from 18 to 30 years made up the experimental or test group. **METHOD:** Investigators tracked the number of reports of cold and flu symptoms among the 1991 test population of the facility compared with the reports of like symptoms among the 1990 control population. Those in the control population reporting symptoms were treated with pain relievers and decongestants, whereas those in the test population reporting symptoms were treated with hourly doses of 1000 mg of Vitamin C for the first 6 hours and then 3 times daily thereafter. Those not reporting symptoms in the test group were also administered 1000-mg doses 3 times daily. **RESULTS:** Overall, reported flu and cold symptoms in the test group decreased 85% compared with the control group after the administration of megadose Vitamin C. **CONCLUSION:** Vitamin C in megadoses administered before or after the appearance of cold and flu symptoms relieved and prevented the symptoms in the test population compared with the control group.

J Manipulative Physiol Ther 1999 Oct;22(8):530-3

Effects of high dose vitamin C treatment on Helicobacter pylori infection and total vitamin C concentration in gastric juice

Low gastric juice total vitamin C concentration in the presence of Helicobacter pylori (H. pylori) infection probably plays a role in gastric carcinogenesis. In vitro vitamin C has been shown to inhibit the growth of H. pylori. The aims of this study were to determine the effect of high dose vitamin C administration on H. pylori infection and on gastric juice total vitamin C concentration in patients with H. pylori related chronic gastritis. Sixty patients with dyspeptic symptoms and proven chronic gastritis and H. pylori infection, who were undergoing routine endoscopy, entered the study after giving informed consent. They were randomly coded into two treatment groups. Group 1 (controls, n = 28) were treated with antacids for 4 weeks and Group 2 (n = 32) received vitamin C 5g daily also for 4 weeks. Nine patients did not complete the study and were excluded. Plasma and gastric juice total vitamin C levels were measured at baseline, at the end of 4 weeks treatment and again 4 weeks after treatment cessation. In the control group H. pylori infection remained unchanged in all 24 patients throughout as did the mean gastric juice total vitamin C concentration. However, in the vitamin C treated group eight of 27 patients (30%) who completed the treatment course the H. pylori infection was eradicated (P = 0.01). In these patients the mean gastric juice total vitamin C concentration rose significantly from 7.2 +/- 1.6 micrograms/ml after 4 weeks treatment (P < M 0.001) and 19.8 micrograms/ml 4 weeks after treatment was discontinued (P < 0.001). In the remaining 19 patients with persistent H. pylori infection, the mean gastric juice total vitamin C concentration rose less than in those with successful H. pylori eradication; 6.3 +/- 1.7 micrograms/ml before treatment, 10.8 +/- 1.5 micrograms/ml after 4 weeks treatment (P < 0.05) and a return to pre-treatment levels (7.1 +/- 2.7 micrograms/ml) 4 weeks after vitamin C intake stopped. There were no side effects of vitamin C treatment. This study has shown that 4 weeks daily high dose vitamin C treatment in H. pylori infected patients with chronic gastritis resulted in apparent H. pylori eradication in 30% of those treated. In those patients there was also a highly significant rise in gastric juice total vitamin C concentration which persisted for at least 4 weeks after the treatment ceased. A significant, though less marked, gastric juice total vitamin C concentration increase was observed during vitamin C treatment even in subjects with persistent H. pylori infection, though this was not maintained after treatment ended. The mechanism whereby vitamin C treatment appeared to result in H. pylori eradication is unclear. Further confirmatory studies are indicated.

Eur J Cancer Prev 1998 Dec;7(6):449-54

Silibinin/Silymarin

The effect of silibinin (Legalon) on the the free radical scavenger mechanisms of human erythrocytes in vitro

The effect of Legalon was investigated parallel with that of Adriblastina (doxorubicin) and paracetamol on some parameters characterizing the free radical scavenger mechanisms of human erythrocytes in vitro and on the time of acid hemolysis performed in aggregometer. Observations suggest that Adriblastina enhances the lipid peroxidation of the membrane of red blood cells, while paracetamol causes significant depletion of intracellular glutathione level, thus decreasing the free radical eliminating capacity of the glutathione peroxidase system. Legalon on the other hand, is able to increase the activity of both superoxide dismutase and glutathione peroxidase, which may explain the protective effect of the drug against free radicals and also the stabilizing effect on the red blood cell membrane, shown by the increase of the time of full haemolysis.

Acta Physiol Hung 1992;80(1-4):375-80

Endogenous mono-ADP-ribosylation in retina and peripheral nervous system. Effects of diabetes

The extranuclear endogenous mono-ADP-ribosylation of proteins was monitored in cellular preparations of retina, superior cervical ganglion, dorsal root ganglia and peripheral nerve. At least 6 protein fractions are ADP-ribosylated in the crude extract fraction from retina control preparations, while in diabetic rats the number of retina labeled proteins and the extent of labeling are highly reduced. In the superior cervical ganglion labeling was present in 10 proteins, in diabetics it was greatly decreased. Treatment of diabetic rats with silybin, a flavonoid mono-ADP-ribosyltransferase inhibitor, did not affect hyperglycemia, but prevented the alteration of extent of protein ADP-ribosylation. These data suggest that proteins of retina and peripheral ganglia are excessively ADP-ribosylated in vivo. The effects of silybin treatment on excessive mono-ADP-ribosylation of proteins was associated with the prevention of reduction of substance P-like immunoreactivity levels, that is typical of diabetic neuropathy. In the membrane fraction of sciatic nerve Schwann cells, at least 9 proteins were ADP-ribosylated, diabetes caused a marked increase of labeling. A comparable increase involving the same proteins is triggered by chronic nerve injury and by corticosteroid treatment. Silybin treatment of diabetic rats prevented such an increase. We propose that the inhibition of excessive protein mono-ADP-ribosylation by silybin prevented the onset of diabetic neuropathy. While the effects on Schwann cells is likely indirect and secondary to the improvement of diabetic axonopathy.

Adv Exp Med Biol 1997;419:289-95

Silymarin retards collagen accumulation in early and advanced biliary fibrosis secondary to complete bile duct obliteration in rats

Silymarin (SIL), a standardized plant extract containing about 60% polyphenole silibinin, is used as a hepatoprotective agent. Its antifibrotic potential in chronic liver diseases has not been explored. Therefore, we applied SIL to adult Wistar rats that were subjected to complete bile duct occlusion (BDO) by injection of sodium amidotrizoate (Ethibloc). This treatment induces progressive portal fibrosis without significant inflammation. Rats with sham-operation that received SIL at 50 mg/kg/d ($n = 10$) and rats with BDO alone ($n = 20$) served as controls, whereas groups of 20 animals were fed SIL at a dose of 25 and 50 mg/kg/d during weeks 1 through 6 or doses of 50 mg/kg/d during weeks 4 through 6 of BDO. Animals were sacrificed after 6 weeks for determination of blood chemistries, total and relative liver collagen (as hydroxyproline [HYP]), and the serum aminoterminal propeptide of procollagen type III (PIIINP). BDO in untreated rats caused an almost ninefold increase in total liver collagen (16.1 ± 3.1 vs. 1.8 ± 0.4 mg HYP, $P < .001$). SIL at 50 mg/kg/d reduced total HYP by 30% to 35%, either when given from week 1 through 6 or from week 4 through 6 after BDO (10.6 ± 2.7 and 10.2 ± 3.9 mg HYP, both $P < .01$ vs. BDO alone), whereas 25 mg/kg/d were ineffective. Because SIL at 50 mg/kg/d also reduced the collagen content per gram of liver tissue, it acted as a true antifibrotic agent. The single value of PIIINP at killing paralleled the antifibrotic activity of SIL with 11.6 ± 3.8 and 9.9 ± 3.7 vs. 15.3 ± 5.2 microg/L in both high-dose groups ($P < .05$ and $P < .01$, respectively, vs. rats with BDO alone). Except for a decreased alkaline phosphatase and a lower histological fibrosis score in the groups that received SIL, clinical-chemical parameters were not different among all groups with BDO. We therefore conclude that 1) BDO with Ethibloc is a suitable model to test for pure antifibrotic drugs because it induces progressive rat secondary biliary fibrosis without major inflammation; 2) oral SIL can ameliorate hepatic collagen accumulation even in advanced (biliary) fibrosis; and 3) PIIINP appears to be a suitable serum marker to monitor the inhibition of hepatic fibrogenesis in this model of biliary fibrosis.

Hepatology 1997 Sep;26(3):643-9

Randomized controlled trial of silymarin treatment in patients with cirrhosis of the liver

Silymarin, the active principle of the milk thistle *Silybum marianum*, protects experimental animals against various hepatotoxic substances. To determine the effect of silymarin on the outcome of patients with cirrhosis, a double blind, prospective, randomized study was performed in 170 patients with cirrhosis. 87 patients (alcoholic 46, non-alcoholic 41; 61 male, 26 female; Child A, 47; B, 37; C, 3; mean age 57) received 140 mg silymarin three times daily. 83 patients (alcoholic 45, non-alcoholic 38; 62 male, 21 female; Child A, 42; B, 32; C, 9; mean age 58) received a placebo. Non-compliant patients and patients who failed to come to a control were considered as 'drop outs' and were withdrawn from the study. All patients received the same treatment until the last patient entered had finished 2-years of treatment. The mean observation period was 41 months. There were 10 drop outs in the placebo group and 14 in the treatment group. In the placebo group, 37 (+2 drop outs) patients had died, and in 31 of these, death was related to liver disease. In the treatment group, 24 (+4 drop outs) had died, and in 18 of these, death was related to liver disease. The 4-year survival rate was 58 +/- 9% (S.E.) in silymarin-treated patients and 39 +/- 9% in the placebo group ($P = 0.036$). Analysis of subgroups indicated that treatment was effective in patients with alcoholic cirrhosis ($P = 0.01$) and in patients initially rated 'Child A' ($P = 0.03$). No side effects of drug treatment were observed.

J Hepatol 1989 Jul;9(1):105-13

Liver-protective action of silymarin therapy in chronic alcoholic liver diseases

The effects of silymarin (Legalon) therapy on liver function tests, serum procollagen III peptide level and liver histology were studied in 36 patients with chronic alcoholic liver disease in a six month double blind clinical trial. During silymarin treatment serum bilirubin, aspartate aminotransferase and alanin-aminotransferase values have been normalized, while gamma-glutamyl transferase activity and procollagen III peptid level decreased. The changes were significant, and there was a significant difference between post-treatment values of the two groups, as well. In the placebo group only gamma-glutamyl transferase values decreased significantly but to a lesser extent than that in the silymarin group. The histological alterations showed an improvement in the silymarin group, while remained unchanged in the placebo group. These results indicate that silymarin exerts hepatoprotective activity and is able to improve liver functions in alcoholic patients.

Orv Hetil 1989 Dec 17;130(51):2723-7

Effect of silibinin on the activity and expression of superoxide dismutase in lymphocytes from patients with chronic alcoholic liver disease

The in vitro and in vivo effects of the naturally occurring flavolignan hepatoprotective agent silibinin on the expression and activity of superoxide dismutase (SOD) enzyme were studied in lymphocytes from patients with chronic alcoholic liver disease. In vitro incubation with silibinin in a concentration corresponding to the usual therapeutic dosage markedly increased the SOD-expression of lymphocytes as measured by flow-cytofluorimetry following staining with monoclonal anti-Cu, Zn-SOD-antibody and FITC-conjugated anti-mouse Ig. In vivo treatment with the drug restored the originally low SOD activity of the patients' lymphocytes. These data indirectly suggest that antioxidant activity might be one of the important factors in the hepatoprotective action of silibinin.

Free Radic Res Commun 1987;3(6):373-7

Scavenging of reactive oxygen species and inhibition of arachidonic acid metabolism by silibinin in human cells

The effects of the flavonoid silibinin, which is used for the treatment of liver diseases, on the formation of reactive oxygen species and eicosanoids by human platelets, white blood and endothelial cells were studied. Silibinin proved to be a strong scavenger of HOCl (IC50 7 microM), but not of O2- (IC50 > 200 microM) produced by human granulocytes. The formation of leukotrienes via the 5-lipoxygenase pathway was strongly inhibited. In human granulocytes IC50-values of 15 microM and 14.5 microM silibinin were detected for LTB4 and LTC4/D4/E4/F4 formation, respectively. In contrast to this, three- to fourfold silibinin concentrations were necessary to half maximally inhibit the cyclooxygenase pathway. For PGE2 formation by human monocytes an IC50-value of 45 microM silibinin was found. IC50-values of 69 microM and 52 microM silibinin were determined for the inhibition of TXB2 formation by human thrombocytes and of 6-K-PGF1 alpha formation by human omentum endothelial cells, respectively. Thus, the deleterious effects of HOCl that can lead to cell death, and those of leukotrienes that are especially important in inflammatory reactions, can be inhibited by silibinin in concentrations that are reached in vivo after the usual clinical dose. Silibinin is thought not only to display hepatoprotective properties but might also be cytoprotective in other organs and tissues.

Life Sci 1996;58(18):1591-600

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

LifeExtension®

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.