Naturopathic Perspectives

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Liver Support: An Evidence-Based Review & Call for Research

In Complementary and Alternative medicine (CAM), practitioners often speak of and employ "liver support." Liver supportive therapies are widely used and incorporate the use of several different forms of natural medicines including herbs, vitamins, minerals, amino acids and organ extracts. Liver support entails the use of therapies that assist the liver in carrying out its biologic functions as well as prevention and repair of damage to this organ. Too often, critics of CAM therapies argue that research is lacking which explores the effectiveness and evidence of natural medicines, especially those that work more along the lines of a functional medicine approach. That is, medicine which seeks to improve or assist the function of an organ or organ system by supporting its physiologic function. This criticism is valid and at the same time lacking in accuracy. True, much evidence exists exploring (and demonstrating) the effects of natural medicines on various health conditions. More importantly however, additional exploration is needed into this area as well as the occurrence of synergism between natural medicines. Synergy between nutrients and herbs is an important, yet underexplored aspect of CAM medicine. It is imperative that as practitioners of natural medicine, we all help contribute to the building of the scientific evidence of the clinical usefulness and create the foundation for further exploration of benefits of synergy.

The purpose of this article is to highlight the evidence behind several liver supportive medicines, as well as a call for office-based research employing a synergistic blend of liver supportive medicines. In order to stimulate more office-based research using natural therapies, trial samples of a liver support product, *Liver C/S Plus™*, are available (free of charge) to clinicians treating patients with liver conditions. (See table 1). In exchange for a supply of *Liver C/S Plus™*, investigators request that pertinent data regarding clinical outcomes is completed using a brief, 2-page document provided by the manufacturer of *Liver C/S Plus.™*

While already on the market and available, more evidence is desired to further define the efficacy of this product in supporting healthy liver function. More information regarding samples of *Liver C/S Plus™* and this ongoing research trial is provided at the end of this article.

Reasoning for using liver supportive therapies

As the second largest detoxification organ in the body, and the only one with highly specific regenerative capacities, the liver is constantly bombarded with nutrients, toxins, drugs, and many other substances entering the body as part of its role in detoxification, a vital role in human health. People today are under constant assault from toxic substances in our environment. From pesticide and industrial chemical residues to xenoestrogens, preservatives, and even pharmaceuticals, our bodies face an ever-growing challenge to remove these toxins, not to mention dealing with pathologies like viral hepatitis.

A damaged or diseased liver leaves us more susceptible to infections, compromises our digestion and saps us of vital energy. Accumulated toxins in the body place a constant drag on the immune system, setting the stage for autoimmune diseases and cancer. If any one organ is compromised, others will be affected eventually, leading to a cumulative negative effect on health. Today's advanced medical practitioners know that health promotion and disease prevention will dominate the future of medicine, rather than reactive medicine that only addresses disease once it has occurred. The use of liver supportive therapies is typically used in order to:

- Help cleanse, protect and rejuvenate liver tissue
- Improve digestion and elimination by supporting liver function
- Enhance energy, vitality and well-being by increasing functional liver health
- Help repair and regenerate liver cells through improved liver-specific nutrition
- Enhance absorption of vital nutrients via lipotropic factors

More specifically, several different nutraceuticals and herbs have proven benefits on liver function.

Alpha-lipoic acid

A powerful fat and water soluble antioxidant, Alpha lipoic acid (ALA) drives glutathione production in liver, promotes detoxification and regeneration and exerts a stabilizing influence on blood sugar levels. ALA serves to regenerate antioxidant molecules in the body such as vitamin E, vitamin C and glutathione leading to decreased oxidative damage.[1] In certain liver diseases (alcohol-induced damage, mushroom poisoning, metal intoxification, and carbon tetrachloride poisoning) oxidative stress may certainly be a factor making ALA an appropriate preventive intervention.[2] Additionally, ALA has been used with success in prevention of poisoning from arsenic, cadmium, mercury and lead, aminoglycosides, and hexachlorobenzene and n-hexane.[3-6] Other evidence shows that ALA may improve the antioxidant levels in blood while decreasing the amount of peroxidation products of lipids and proteins and increase the ratio of T-helper lymphocytes to T- ➤

Table 1: Liver Conditions Treated with Liver Support

Alcoholic Liver disease:	Hepatitis C
• Fatty Liver (Steatosis)	Hepatocellular carcinoma
• Hepatitis	Gilbert's syndrome
• Cirrhosis	Rotor syndrome
Non-alcoholic cirrhosis	Sclerosing cholangitis
Non-alcoholic steatosis	Wilson's disease
Non-alcoholic steatohepatitis	Budd-Chiari syndrome
Hepatitis A	Liver Transplantation
Hepatitis B	General liver health/support
Hepatitis B & D	

➤

helper suppressor lymphocytes in patients with human immunodeficiency virus (HIV).[7]

Phosphatidyl choline

A phospholipid molecule and primary component of lecithin, phosphatidyl choline (PC) emulsifies fat deposits in the liver thereby assisting transportation out of this organ. PC, once hydrolyzed, is thought to play a direct role in regulating specific fats as well as fat-soluble vitamins[8]; it is also thought to protect against liver fibrosis and oxidative stress induced by alcohol.[9] PC acts as an antioxidant as well,[10] and in both human and animal studies it was protective against several different chemical toxins and adverse pharmaceutical effects.[11] A review article of the clinical benefits of PC postulated that treatment with PC resulted in consistent clinical improvements including improved structural repair and function of the liver, improved enzymatic and other biologic indicators, as well as improvements in study subjects' well-being and survival.[12]

In the treatment of alcoholic hepatic steatosis, PC has been shown to provide promising effects: 40 subjects with hepatic steatosis (fatty liver) that was linked to alcohol intake were treated using PC with promising results.[13] Study subjects showed improvement within two weeks of therapy using PC and at 8 weeks of therapy, liver function measures were improved greater than those treated with placebo. Other trials have documented success using PC in liver diseases.[14,15]

Other studies have shown benefit from using PC in the treatment of hepatitis B. In subjects with chronic hepatitis B, those treated with PC demonstrated stabilization with significant improvement of liver parenchymal structure at one year in comparison to similar subjects treated with placebo (placebo group worsened over the year-long time frame of the study).[16] Another trial utilizing patients with severe liver damage from hepatitis (HbsAg-positive) showed remarkable improvement in these subjects after undergoing treatment with PC[17]; 80% of subjects were deemed greatly improved (as determined by cell-structure, biochemical, immunologic, and hematologic parameters) compared to 24% of placebo subjects who were deemed moderately improved. Of those who demonstrated improvement, clinical benefit continued beyond the time frame of the study. The use of PC in cases of hepatitis C has shown benefit as well.[18]

Inositol

Sometimes referred to as vitamin B-8, inositol is a component of the phospholipid structure in cell membranes. It is useful in liver conditions for breaking down fats and lowering cholesterol levels, thereby reducing the overall liver burden. Inositol does have lipotropic (fat-loving) activity, moving fat out of the liver.[19] Simply put, lipotropics are substances that can liquefy or homogenize fats, assisting in their transportation in the body. By solubilizing cholesterol, this leads to lower levels of cholesterol in the blood vessels and lowers the ability of gallstones to form, further slowing liver function. By preventing the accumulation of fats in the liver, this organ is better able to function correctly.

Milk Thistle Seed (Silybum marianum)

A traditional liver herb with established protective and detoxification effects on the liver, milk thistle has been shown to prevent damage from toxic substances and stimulate protein synthesis to accelerate the production and regeneration of liver cells. Liver disorders in which milk thistle has shown benefit include chemical damage, Amanita mushroom poisoning, jaundice, chronic hepatitis, liver cirrhosis, and chronic inflammatory liver disease. Milk thistle is also beneficial in liver patients with lack of appetite. The main active constituent of milk thistle, silymarin, is subjected to recirculation in the intestinal-liver circulatory pathways (enterohepatic) and is found in higher concentrations in liver cells.

Silymarin has several possible effects in modulating liver disease. It is thought that silymarin induces an alteration in the outer cell membrane of liver cells leading to increased resistance against toxin penetration; it is also thought to have antifibrotic, antiinflammatory and immune boosting functions that are helpful in liver conditions.[20]

Silymarin has the ability to inhibit the enzyme beta-glucuronidase and in doing so may prevent hepatic cellular injury by reducing the conversion of glucuronide conjugates into toxic metabolites in the liver and intestine.[21] One highly fascinating property of silymarin is its ability to generate production of nucleolar polymerase A, which results in ribosomal protein synthesis – stimulating liver regeneration and new cellular production.

Turmeric (Curcuma longa)

Turmeric is a traditional Indian liver herb that stimulates the gallbladder and has antioxidative, antiinflammatory, anti-fungal and anti-bacterial properties. A digestive aid, turmeric is thought to have anti-cancer properties as well. The main active constituent of turmeric is curcumin, a yellow colored pigment. The antiinflammatory effects of this herb are attributable to its ability to inhibit the cyclooxygenase-2 enzyme, inflammatory leukotrienes and prostaglandins.[22,23] The immunostimulatory effects of curcumin include the ability to increase white cell counts, antibody titers, and bone marrow cellular density. Additionally, curcumin caused a significant increase in macrophage activity in laboratory animals.[24] The anticancer effects of curcumin include inhibition of growth against certain tumors and other chemopreventive actions.[25]

A trial involving curcumin as a preventive agent in alcohol-induced liver injury demonstrated the ability of curcumin to circumvent commonly associated alcohol-induced elevations in liver enzymes and lipid peroxidative compounds.[26] Investigators conclude that curcumin exerts its protective effects by improving antioxidant status and decreasing oxidation of fats in the liver.

Dandelion root (Taraxacum officinale)

A liver-specific herb with diuretic and bile forming properties, dandelion can assist in the removal of toxins from the body, and has very gentle laxative properties which further assist in toxin removal. One constituent of dandelion, taraxacin, exerts beneficial effects on the digestive process; the bitter parts of the root can effect increased bile flow.[27] Dandelion has been used traditionally as a diuretic. In laboratory animals, an extract of dandelion leaf showed comparable diuretic activity to furosemide.[28] These animals lost nearly 30% of their body weight over a period of 30 days; much of this weight loss is attributed to diuresis from Taraxacum.

Artichoke (Cynara scolymus)

Known for its abilty to lower serum cholesterol and triglycerides, artichoke also promotes liver cell regeneration and improves digestion. The medicinal parts of the artichoke include the leaves, stem and root. Some of the primary active constituents are cynarin, chlorogenic acid, caffeic acid and polyphenol and flavonoid compounds.[29] One of the main benefits of artichoke is its choleretic (stimulation of bile flow) effect. This ability has been shown in several different studies; the constituents responsible for this action are chlorogenic acid and cynarin. Additionally, cynarin and chlorogenic acid may lower cholesterol[30]

and even inhibit the syntheis of cholesterol as well.[31] It is thought that cynaroside, another active constituent of artichoke, has the ability to indirectly inhibit the enzyme HMG-CoA reductase, the key enzyme in cholesterol biosynthesis.[32] Other benefits of artichoke on the liver include antioxidant activity,[33] and the ability to protect hepatic cells from damage.[34] Several of the active constituents of artichoke (flavonoids and polyphenols) are thought to provide the hepatoprotective effects. These liver-specific actions make artichoke a necessary treatment in all liver conditions.

Other Liver Supportive Botanicals

Several other liver supportive botanical medicines are contained in *Liver C/S Plus™* due to their historical and modern application in liver conditions. **Schizandra** fruit is a Chinese remedy used for thousands of years to improve stamina, as a liver protectant, and adaptogenic herb. Modern research has demonstrated the powerful hepatoprotective functions of this fruit by its ability to increase the amount of antioxidants produced in the liver (glucose-6-phosphate, glutathione-reductase, and glutathione activity). Other liver protective effects of Schizandra include the ability to increase liver glycogen production, slowing free radical formation and damage, as well as enhancing the growth of liver cells.[35] **Bupleurum Root** is another traditional Chinese herb used to reduce liver inflammation and increase protein synthesis with demonstrated hepatoprotective,[36] antimicrobial, and potent liver supportive effects.[36]

Andrographis Paniculata and ***Picrorhiza Kurroa*** are both Ayurvedic herbs with long histories of use in treating liver conditions. Andrographis is known historically as a liver tonic and has been shown to have hepatoprotective effects by increasing bile flow and promoting liver health. In fact, an extract of the herb, known as andrographolide has been shown to be a more potent hepatoprotectant than silymarin in laboratory animals.[37] Picrorhiza has a history of use in protecting and support liver function, and has been shown to be hepatoprotective and exert beneficial effects on common liver function measures.[38] Newer evidence points to the ability of Picrorhiza to protect the liver against agents such as ethanol and the Amanita mushroom.[39,40]

A Call for Research

The natural medicines highlighted above are employed often in the treatment of liver conditions, but rarely all at the same time in synergistic fashion. Practitioners now have the opportunity to use these medicines, in one combination, for their patients in need of liver supportive therapies. The above is only a brief review of the research on each individual compound; unified application of these medicines may greatly enhance patient outcomes. By participating in this study, a limited supply of this product is available, without cost to the practitioner or patient in order to establish the effects of these synergistically arranged nutrients in liver conditions. Health care practitioners are invited to participate in a multicenter trial using a liver supportive combination therapy. Details of this investigation are available from the manufacturer of *Liver C/S Plus™*. All inquiries may be directed to: John Burgstiner, Preventive Therapeutics, Inc. 2020 Westside Court, Suite A, Snellville, Georgia 30078 USA, 800-556-5530.

Conflict of interest: The authors have no financial interest in Preventive Therapeutics, Inc. (PTI) or Liver C/S Plus™ and derive no financial incentive from future sales of this or any other PTI product. The authors participated in the design of the Liver C/S Plus™ clinical study and serve as co-investigators.

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