Natural Lipotropic Agents for Improved Liver Function

Scott Luper reviews the role of several natural products which have been used clinically to support liver function.

Review of Natural Lipotropic Agents, Hepatoprotectants and Cholegogues in Liver Function.

Scott Luper, ND

Introduction

A number of acquired conditions can adversely affect liver function. Excessive dietary intake of fat, alcohol and simple carbohydrates can lead to fatty infiltration and compromised function of the liver. Exposure to ethanol, certain drugs and other xenobiotics can result from malabsorption, impaired peristalsis, decreased vagal stimulation and other disorders. These conditions can lead to impaired fat digestion and further malabsorption of nutrients.

Research indicates that lipotropic agents such as methionine and choline can aid hepatic fat metabolism and mobilization of fats from the liver. Silymarin has been shown to prevent hepatocellular damage in human and animal studies. Recent research supports the traditional use of herbs including Taraxacum officinale, Chelidonium majus, and Beta vulgaris. This review examines the role of several natural agents which have been used clinically to support liver function.

Hepatoprotective effects of Silymarin

Silymarin is a naturally occurring phytochemical extracted from Milk Thistle seed (Silybum marianum). Research has shown that Silymarin protects the liver from a wide variety of insults including carbon tetrachloride and acetaminophen toxicity, radiation, ischemia, mushroom poisoning, and other sources of free radicals. The hepatoprotective effects of silymarin stem largely from its antioxidant properties.

A study in 1994 reported on mushroom poisoning that occurred in 25 of 36 individuals who ingested Amanita gemmata mushrooms. All 25 experienced acute gastroenteritis that was followed in seven by acute hepatitis and in one by a massive upper gastrointestinal bleeding. Three subjects with fulminant hepatic failure and the subject with the massive bleeding died. The patients were treated with silymarin and penicillin G. The authors attribute the benefits of the treatment to the antitoxic effects.
Sierralta A. Jeria ME. Fugueroa G. Pinto J. Araya JC. San Juan J. Grinbergs J. Valenzuela E., [Mushroom poisoning in the IX region. Role of Amanita femmata]. [Spanish] Intoxicacion por callampas venenosas en la IX region. Rol de Amanita gemmata. *Revista Medica de Chile.* **122(7):795-802,1994.**

A 1993 study described a case of severe mushroom poisoning in a 7 year old girl resulting in hepatic coma with the prothrombin-time less than 10% of the normal values. She was treated with silymarin and penicillin G. The authors attribute the favorable outcome of the case to the treatment.
Rambousek V, Janda J, Sikut M, [Severe Amanita phalloides poisoning in a 7-year-old girl]. Tezka otrava muchomukou hlizovitou u sedmilete divky.
Ceskoslovenska Pediatrie. **48(6):332-3, 1993.**

Effects of Silymarin in Acetaminophen Intoxication

A 1992 study examined the effect of silymarin on liver damage in rats induced by acetaminopohen (APAP) intoxication. Reduced glutathione (GSH), lipid peroxidation and glycogen were measured in liver and alkaline phosphatase (AP), gamma-glutamyl transpeptidase (GGTP) and glutamic pyruvic transaminase (GPT) activities were measured in serum. After APAP intoxication, GSH and glycogen decreased and remained low for 6 h. Lipid peroxidation increased three times over the control 4 and 6 h after APAP treatment. Enzyme activities increased 18 h after intoxication. In the group receiving APAP plus silymarin, levels of lipid peroxidation and serum enzyme activities remained within the control values. It was concluded that silymarin can protect against APAP intoxication through its antioxidant properties, possibly acting as a free-radical scavenger.

Muriel P, Garciapina T, Perez-Alvarez V, Mourelle M, Silymarin protects against paracetamol-induced lipid peroxidation and liver damage. ***Journal of Applied Toxicolgy.*** **12(6);439-42, 1992.**

Silymarin's Protective Effect on Radiation Damage

Investigators measured the influence of silymarin on radiation-induced changes in concentrations of RNA and DNA in male Wistar rats. The liver, spleen and bone marrow were examined at 30 h, 7, 14 and 21 days after 6 Gy whole-body gamma irradiation or 30 h and 7 days after 3 Gy whole-body gamma irradiation. Silymarin administered 1 h before irradiation moderated radiation-induced changes in nucleic acids in target organs, liver, spleen and bone marrow. The authors suggest that beneficial effects of silymarin on radiation injury to the membranes of liver cells resulted primarily from its antioxidant properties and its ability to act as a free radical scavenger, thereby preventing permeability changes and membrane damage.

Hakova H, Misurova E, The effect of silymarin and gamma radiation on nucleic acids in rats organs. ***Journal of Pharmacy & Pharmacology.*** **45(10): 910-2, 1993.**

Methionine and Cirrhosis of the Liver

Methionine metabolism impairment in human liver disease has been related to an alteration in SAM-synthetase. A series of different experiments on the structure and activity of this enzyme have provided strong evidence that SAM-synthetase is regulated by reduced/oxidized glutathione ratio. Restoration of glutathione levels by the addition of S-adenosyl-methionine or glutathione esters in various experimental conditions (buthionine sulfoximine and carbon tetrachloride intoxication) resulted in a normalization of the SAM-synthetase diminution caused by the toxics and an attenuation of the morphological alteration produced in the liver, including fiber production. These findings might have pharmacological implications in the treatment of liver diseases, since the possible beneficial effect of long term administration of SAM could include a reduction in liver fibrosis.

Mato JM, Alvarez L, Ortiz P, Mingorance J, Duran C, Pajares MA, S-adenolyl-L-methionine sythetase and methionine metabolism deficiencies in cirrhosis. ***Advances in Experimental Medicine & Biology.*** **368:113-7, 1994.**

Methionine and Alcohol Metabolism

This paper reviews some recent findings in the author's laboratory, which demonstrate that ethanol feeding to rats impairs the folate-induced reaction. The author's findings show that this impairment is compensated for through the adaptive increase in the enzyme using betaine in the biosynthesis of methionine. Further studies indicate that the mechanism of action in the impairment may occur through the formation of individual adducts between the folate-induced enzyme (methionine sythetase), its essential cofactors and acetaldehyde, a metabolic product of ethanol. These findings suggest a basis for why rats are more resistant to alcoholic liver injury than humans and may offer a means of protecting against alcoholic liver injury in man.

Barak AJ, Beckenhauer HC, The influence of ethanol on hepatic transmethylation. ***Alcohol & Alcoholism.*** **23(1);73-7, 1988.**

The Role of Choline in Liver Function

This paper reviews the functions and necessity of dietary choline in humans. The authors review the functions of choline which include methyl group metabolism, lipid transport, membrane phospholipid structure, neurotransmitter formation (acetylcholine), and platelet activating factor. They make the argument that choline should be considered an essential nutrient for humans. The argument is supported by recent clinical studies showing choline to e essential for normal liver function. Also, evidence from the fields of molecular and cell biology shows that certain phospholipids play a critical role in generating second messengers for cell membrane signal transduction. Disruptions in phospholipid metabolism can interfere with this process and may underlie certain disease states such as cancer and Alzheimer's disease.

Canty DJ, Zeisel SH, Lecithin and choline in human health and disease. ***Nutrition Reveiws.*** **52(10):327-39, 1994.**

Choline Deficiency and Liver Disease

In this review the authors explore the relationship between choline deficiency and liver disease. The authors state that the pathologic consequences of feeding a choline deficient diet are fatty liver, liver cell death, liver cell proliferation, and liver cell cancer. Fatty liver due to choline deficiency appears to occur via interference with hepatic VLDL production and output. This I believed to be the mechanism of other forms of fatty degeneration. The induction of cell death appears to be consistent with an increase in liver free radicals leading to both acute necrosis and initiation of carcinogenesis. The feeding of the choline deficient diet reproducibly induces severe and persistent fatty liver coupled with extensive cell death, a combination that has been associated with the development of "micronodular" (fatty) cirrhosis in humans.

Ghoshal AK, Farber E, Cholilne deficiency, lipotrope deficiency and the development of liver disease including liver cancer: a new perspective. ***Laboratory Investigation.*** **68(3)255-60, 1993.**

Cholegogue Effects of Taraxacum Officinale

Research with humans and laboratory animals have shown that Taraxacum enhances the flow of bile. Improved bile flow can benefit conditions such as liver congestion, bile duct inflammation, hepatitis, gallstones and jaundice. Taraxacum's action is twofold; it has a direct effect on the liver, causing an increase in bile production and flow to the gallbladder (choleretic effect), and a direct effect on the gallbladder, causing contraction and releases of stored bile (cholegogue effect). Taraxacum's beneficial effect on such a wide variety of conditions is probably closely related to its ability to improve the functional capacity of the liver.

Mowry DB, The Scientific Validation of Herbal Medicine. Cormorant Books, Lehi UT, 1986.

Faber K, The Dandilion – Taraxacum officinale. *Weber Pharmazie* 13;423-35, 1958.

Chelidonium majus in Liver Dysfunction

Chelidonium (Celandine) has been traditionally regarded as one of the best remedies for inflammation of the biliary tract. The active principle of chelidonium is the alkaloid chelidonine. Chelidonine is closely related to papaverine and shares its antispasmodic activity. The antispasmodic activity of Chelidonine is directed specifically toward the bile ducts and the brochi. Use of Chelidonium as a cholegogue has been reported in conditions such as liver congestion, bile duct inflammation, hepatitis, gallstones and jaundice.

Weiss RF, Herbal Medicine. Beaconsfield Publishers LTD, Beconsfield, England, 1988.

British Herbal Medicine Association, Scientific Committee: British Herbal Pharmacopoeia. British Herbal Medicine Association, Cowling, England, 1983.

Beta vulgaris

Beta vulgaris (Beet leaf) has been used traditionally to treat conditions of the liver. Research has shown that the beet is high in betaine. Betaine acts on the methylation cycle in the liver cells, functioning as a methyl donor. Betaine assists in the conversion of homocysteine to methionine and eventually to the elevation of S-adenosylmethionine levels. The effect on the liver is to prevent fatty infiltration. Beet leaf has been used traditionally to treat the toxic effects of prolonged alcohol use on the liver. Once again current research has shown that adequate levels of betaine can prevent ethanol-induced fatty liver.

Barak AJ, Beckenhauer HC, Junnila M, Tuma DJ, Dietary betaine promotes generation of hepatic S-adenosylmethionine and protects the liver from ethanol-induced fatty infiltration. *Alcoholism, Clinical & Experimental Research.* 17(3):552-5, 1993 Jun.

Weiss RF, Herbal Medicine. Beaconsfield Publishers LTD, Beaconsfield, England, 1988.