Silymarin for treatment of liver diseases

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In Europe, the milk thistle (Silybum marianum Gaertneri) has been used as a remedy for liver diseases since the 13th century. Silymarin is an extract of this plant, and consists of a mixture of different flavonoids: silibinin (the active ingredient), silicristin and silidianin. The hepatoprotective properties of silibinin against different hepatotoxins are well documented experimentally. Silibinin prevents it in rats the toxic effects of iron overload (Gastro 1995;109:1941), delays collagen accumulation after bile duct algae (Hepatology 1997;26:643). Furthermore, in cell cultures, cold damage to liver cells is mitigated (Hepatology 1997;26:351), a finding that could be important for the preservation of donor organs. The mode of action of silibinin may be antioxidant properties that prevent cell damage by free oxygen radicals, inhibition of leucotrien formation (Hepatology 1996;23:749) or selective inhibition of NF-κB activation (FEBS Letters 1998;440:8). However, the clinical efficacy of silymarin is difficult to demonstrate.

1. There have been few randomised, placebo-controlled studies (RCT) in patients with hepatic cirrhosis. In a study conducted in the ´70-ies in Austria mortality was lower in cirrhotic patients treated with silymarin than with placebo (J Hepatol 1989;9:105). Subgroup analysis indicated that this effect was most marked in patients with alcoholic cirrhosis. A Spanish study conducted 10 years later failed to confirm these results (J. Hepatol 1998; 28:615). Both studies were performed in the “pre-hepatitis C” era. Finally, insulin resistance was reduced in cirrhotic patients treated with silymarin (J. Hepatol 1997; 26:871).
2. Fatty liver (MAFLD) is the leading liver disease of the 21st century. Except for “life-style” modifications there is no established medical therapy. Silymarin was investigated in 2 RCT’s. A study conducted in Malaysia (Clin Gastroenterol Hepatol. 2017;15:1940) showed improvement of fibrosis without change in fat (as proposed by FDA as endpoint). A US study showed no benefit of silymarin (Navarro et al, PLoS 2019). Both studies used 700 mg Silymarin TID.
3. Silibinin given iv. is a potent antiviral against the hepatitis C virus (Gastroenterology. 2008;135:1561) and other RNA-viruses.
4. Silibinin given iv. is used as antidote to amantadine (Amanita phalloides) but there are no proper RCT´S. Silymarin may protect the liver against the toxic effects of certain drugs, environmental toxins, and ethanol.

In summary, silymarin is a potentially beneficial drug for treatment of liver diseases. To further evaluate the efficacy of this drug, dose finding studies and RCT´s in well defined patient populations are needed.