

LIVER & SILYMARIN



Liver Knowledge Base

The liver is the largest internal organ of the human body. The adult human liver normally weighs between 1.0 – 2.3 kilograms (2.2 – 5.0 pounds), and is a soft, pinkish-brown "boomerang shaped" organ.

Its anatomical position in the body is: immediately under the diaphragm on the right side of the upper abdomen. The liver lies on the right of the stomach.

Traditional gross anatomy divided the liver into four lobes based on surface features. One of liver ligaments (the falciform ligament) is visible on the front of the liver. This divides the liver into a left anatomical lobe, and a right anatomical lobe.

If to look at the liver from behind (the visceral surface), there are two additional lobes between the right and left.

The liver is among the few internal human organs capable of natural regeneration of lost tissue; as little as 25% of remaining liver can regenerate into a whole liver again.

Medical terms related to the liver often start in

The bile and bile ducts

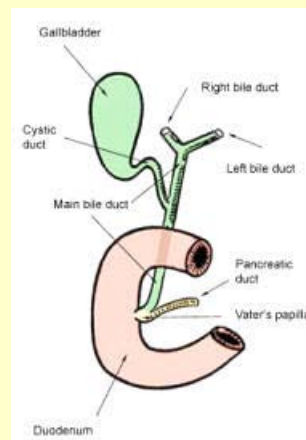
"The bile produced in the liver is collected in bile ductules, which merge next to form bile ducts. These eventually drain into the right and left hepatic ducts, which in turn merge to form the common hepatic duct. The branching of the bile ducts resembles those of a tree, and indeed the term "biliary tree" is commonly used in this setting. It can be temporarily stored in the gallbladder via the cystic duct. The intrahepatic biliary tree is regarded as an excretory duct of two secretory units: hepatocytes (which excrete bile) and intrahepatic peribiliary glands.

INSIDE THIS ISSUE

Liver Knowledge Base	1
The bile and bile ducts	1
Liver Functions & Terms definition	2
Hepatitis	2
Liver Fibrosis	3
Liver Cirrhosis	4
Silymarin	5

hepato- or hepatic from the Greek word for liver, "hepar" (for example, hepatocytes – liver cells), as well as terms related to the bile are from the Greek word for bile, "khole" (for example, cholecystitis, which means inflammation of cholecyst – gallbladder).

The liver is supplied by two major blood vessels: The hepatic artery and the portal vein. The portal vein brings venous blood from the spleen, pancreas, stomach, small and large intestines (except rectum), so that the liver can process the nutrients and byproducts of food digestion; processing of absorbed nutrients and byproducts of food digestion is one of key liver functions for the body.



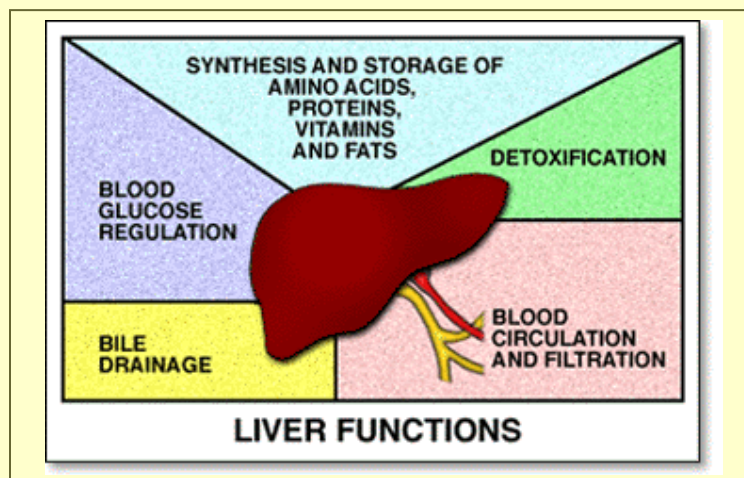
Bile and bile ducts

Liver Functions & Terms definition

Gluconeogenesis: The formation of glucose (blood sugar) from certain amino acids, lactate or glycerol; that is necessary to support the stable concentration of glucose in the blood.

Glycogenolysis: The formation of glucose from glycogen – to mobilize glucose for the body from intrahepatic resource.

Glycogenesis: The formation of glycogen from glucose – to make resource of glucose for future requirement.



Liver Function Diagram

Liver Diseases

Hepatitis

Definition:

Hepatitis means inflammation of the liver.

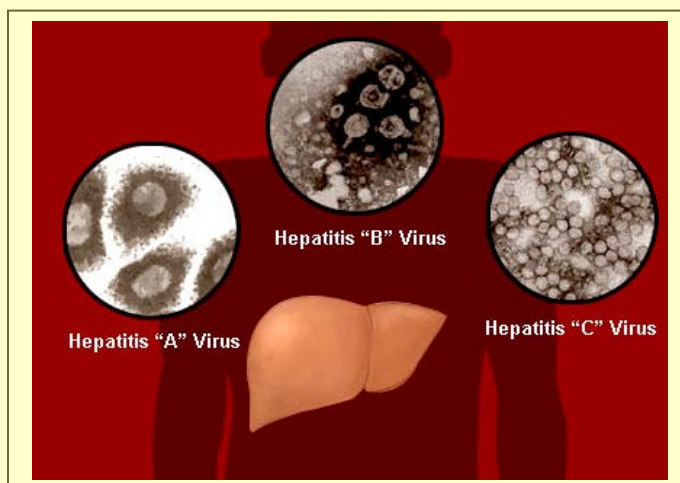
The disease can be caused by:

- ▶ Infections from viruses (such as hepatitis A, hepatitis B, or hepatitis C) or parasites, bacteria;
- ▶ Excess accumulation of fat (triglycerides) in liver cells – Non Alcoholic Fatty Liver Disease (NAFLD) – caused by obesity and abnormal lipid metabolism, may result in Steatohepatitis
- ▶ Liver damage from alcohol, drugs, or poisonous mushrooms
- ▶ Immune cells in the body may attack the liver and cause autoimmune hepatitis
- ▶ Some inherited genetic liver disorders result in hepatitis
- ▶ An overdose of acetaminophen, which is rare but mortal. Besides acetaminophen (other names: Tylenol, paracetamol) some other medications can

cause damage and inflammation of the liver.

Hepatitis may start and resolve quickly (acute hepatitis), or cause long-term disease for decades (chronic hepatitis). In some instances, progressive liver damage, liver failure, or even liver cancer may (hepato-cellular carcinoma) result.

The severity of hepatitis depends on many factors, including the cause of the liver damage and any underlying illnesses you have. Hepatitis A, for example, is generally transient, not leading to chronic liver problems.



Liver Diseases

*"Silymarin Plus Sachets:
Silymarin
N-Acetylcysteine
A group of Antioxidants"*

The symptoms of hepatitis may include some or all of the following (depends on a stage of hepatitis):

- ▶ Early menopause
- ▶ Jaundice (yellowing of the skin or eyes)
- ▶ Weight loss
- ▶ Chronic fatigue
- ▶ Breast development in males
- ▶ Dark urine and pale or clay-colored stools
- ▶ Loss of appetite
- ▶ Abdominal pain or distention
- ▶ General itching
- ▶ Low grade fever
- ▶ Nausea and vomiting

Many people with hepatitis B or C do not have symptoms when first infected and can still develop liver failure later (sometimes decades later).

Chronic hepatitis very often results in liver failure (cirrhosis) or liver cancer.

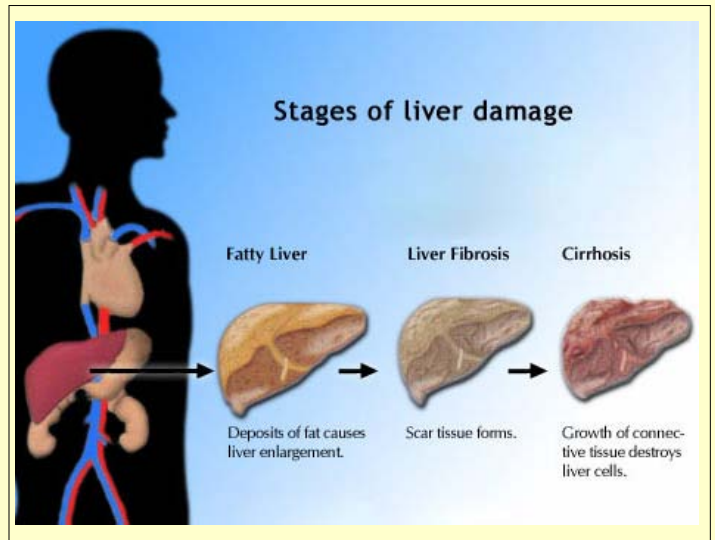
Liver fibrosis

"Fibrosis is the excessive accumulation of extracellular matrix proteins including collagen proteins in abnormal ratio."

In advanced stages, the liver contains approximately 6 times more extracellular matrix proteins than normal and its end-stage disease cirrhosis are major world health problems arising from chronic injury of the liver by a variety of factors including viruses, the metabolic syndrome, autoimmune disease, alcohol and drug abuse, and inherited (genetic) disorders of metabolism.

Cirrhosis is the final common pathway through which nearly all chronic diseases of the liver produce morbidity and mortality.

- ▶ Fibrosis process occurs in most types of chronic liver diseases.
- ▶ It is the consequence of chronic liver injury of any etiology.
- ▶ Hepatic fibrosis is the result of the wound-healing response of the liver to repeated injury.



Historically, treatments for hepatic fibrosis have been directed against specific causes of chronic liver injury, and include for example:

1. Corticosteroids for autoimmune hepatitis
2. Interferon for hepatitis B and C
3. Iron depletion for haemochromatosis
4. Once treatments become ineffective, a liver transplant has been considered until the present.

Transplantation of cultured liver cells:

Transplanted cells stop activated hepatic Cirrhosis, a pathological condition defined by deranged hepatic architecture resulting from progressive fibrosis. Cirrhosis is the final common pathway through which nearly all chronic diseases of the liver produce morbidity and mortality.

Liver cirrhosis

Cirrhosis, a pathological condition defined by deranged hepatic architecture resulting from progressive fibrosis. Cirrhosis is the final common pathway through which nearly all chronic diseases of the liver produce morbidity and mortality.

Complications associated with cirrhosis include:

- **More frequent infections.** If you have cirrhosis, your body may have difficulty fighting infections.
- **Malnutrition.** Cirrhosis may make it more difficult for your body to process nutrients. This can lead to weakness and weight loss.
- **High levels of toxins in the blood (hepatic encephalopathy).** A liver damaged by cirrhosis isn't able to clear toxins from the blood as well as a healthy liver can. Toxins in the blood can cause confusion and difficulty concentrating. With time, hepatic encephalopathy can progress to unresponsiveness or coma.
- **Increasing pressure in the main vein bringing blood to the liver (portal hypertension).** Scar tissue can make it difficult for blood to flow freely through the liver. This causes increased pressure in the portal vein, which causes blood to be redirected to smaller veins near the liver. Those smaller veins may become overwhelmed by the pressure and can burst, causing serious bleeding. Building pressure in the veins of your esophagus is called esophageal varices. In the stomach this is called gastric

Term definitions:

Variceal bleeding:

is caused by portal hypertension, which is an increase in the pressure within the portal vein. This increase in pressure is caused by a blockage of blood flow through the liver as a result of cirrhosis. Increased pressure in the portal vein causes branches of portal vein to enlarge (varices), such as those in the esophagus and stomach, to bypass the blockage. These varices become fragile and can bleed easily, causing severe hemorrhaging and result in fluid buildup in the abdomen.

Confused thinking and other mental changes (Hepatic encephalopathy):

most often occurs when cirrhosis has been present for a long time. Toxins produced in our intestines and ammonia are normally detoxified by the liver, but once cirrhosis occurs, the liver cannot detoxify as well. Toxins get into the bloodstream and can deteriorate brain function and cause confusion, changes in behavior and even coma.

Silymarin Plus

Sachets

"Unique

Composition..

Provides Unique

Protection"

Silymarin

Definition:

Silymarin is an antioxidant flavonoid C₂₅H₂₂O₁₀ consisting of a mixture of three isomers isolated from seeds of the milk thistle, held to have properties protecting the liver from or clearing it of toxins, and used in dietary supplements and herbal remedies .

Scientific Name: Milk Thistle.

Other Names: Cardui mariae, Carduus marianum, Holy Thistle, Lady's Thistle, Legalon, Marian Thistle, Mariendistel, Mary Thistle, Our Lady's Thistle, Silimarina, Silybin, Silybum marianum, St. Mary Thistle.

Clinical study:

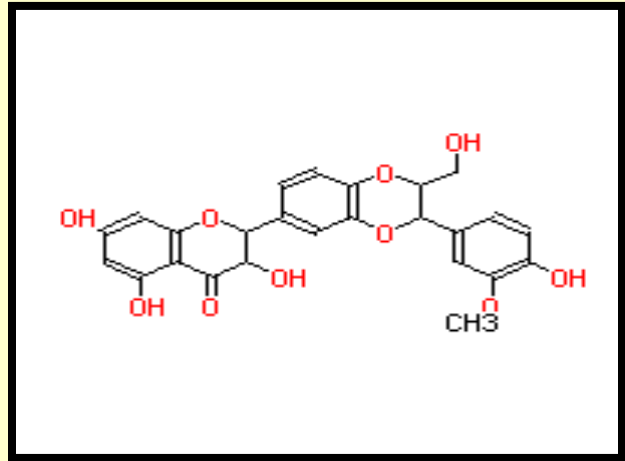
Silymarin provided protection against the toxic effects of long-term treatment with psychotropic drugs (used in mental illness) in a randomized, double-blind, placebo controlled clinical study of 60 people.

Before the study began, all of the participants had been taking the psychotropic drugs phenothiazine or butyrophenone, or both, for at least 5 years. Subjects were divided into four groups for the 3-month trial:

- group I: took psychotropic drugs and a high dose of silymarin (800 mg per day),
- group II: took psychotropic with placebo,
- group III: took silymarin only (800 mg per day),
- group IV: took placebo.

Results: Silymarin provided liver protection to group I by reducing blood levels of malondialdehyde (MDA), an indicator of liver damage that increases during long-term treatment with psychotropics. Not surprisingly, the decrease in MDA levels was even greater in the group taking silymarin alone (group III).

Patients in group II continued to experience rising levels of MDA, whereas those who took placebo in group IV had declining MDA levels until the psychotropics were reinstated. There were no adverse effects associated with Milk Thistle treatment.



The usage of Silymarin:

Milk thistle contains several chemicals with possible medical effects. Most current research focuses on one of them, silymarin, which may have specific protective effects on cells in the liver.

In multiple human, animal, and laboratory studies, silymarin has shown differing degrees of effectiveness for protecting the liver from damage caused by alcohol, chemicals, drugs, diseases, and poisonous plants. It is used to treat both acute conditions (such as poisoning) and long-term diseases (such as hepatitis C).

Silymarin and other chemicals in milk thistle are believed to protect liver cells in several different ways:

- ▶ Silymarin has antioxidant properties. Antioxidants are thought to prevent or lessen damage to body cells that is caused by a chemical process called oxidation.
- ▶ Silymarin as anti-inflammatory effects of help keep liver cells from swelling in response to injury.
- ▶ Silymarin seems to encourage the liver to grow new cells, while discouraging the formation of inactive fibrous tissue.
- ▶ By changing the outside layer of liver cells, silymarin may also keep certain harmful chemicals from getting into liver cells.
- ▶ Silymarin may also cause the immune system to be more active.

► Silymarin and cancer: Silymarin and other chemicals from milk thistle seem to interrupt cancer cell division as well as shortening the time that cancer cells live. They may also stop or limit the formation of new blood vessels that supply tumors. Most research has centered on breast cancer and prostate cancer, but milk thistle is also being tested for treating other cancers such as Leukemia.

Silibinin may even help to restore damaged skin somewhat by mending DNA that has been harmed by ultraviolet rays. In addition, some chemicals from milk thistle may increase the effectiveness of current anticancer drugs.

Some of these anticancer effects are being studied in early-phase human trials, but none is confirmed, yet.

How does Silymarin Work?

An animal study performed in rats demonstrated a reduction in kidney damage following administration of cisplatin without diminished anti-tumor activity.

Other studies indicate the flavonoids in milk thistle has anticancer effects by inducing G1 and S phase arrest in cells.

Especially How It Works for Liver?

Milk thistle provides hepatocellular protection by stabilizing hepatic cell membranes. It alters the structure of the outer cell membrane of the hepatocytes in such a way as to prevent the penetration of the liver toxins into interior of the cell. The stimulation affect on nucleolar polymerase A results in an increase in ribosomal protein synthesis, and thus increase the regenerative ability of the liver and the formation of new hepatocytes. Other actions include interruption of enterohepatic recirculation of toxins and regeneration of damaged hepatocytes.

Prevents toxins from entering the liver by guarding the organ's numerous doorways—the membranes of liver cells. By slowing the rate at which the liver absorbs harmful substances, the toxins are excreted through the kidneys before they can cause liver damage.

Protective effect due to the flavonoid complex silymarin, which acts as a powerful antioxidant, combining with and thus neutralizing harmful free radicals that result from normal metabolic processes and from the breakdown of toxic substances.

Because silymarin is a potent antioxidant in the stomach and intestines, it may also have a role to play in treating inflammatory conditions such as colitis and ulcers.

Silymarin (milk thistle) reverses liver cell damage, increases protein level..... It destroys old red blood cells, produces lymphocytes and plasma cells.

When damage has already been done, Milk Thistle aids the liver in repairing injured cells and generating new ones. It does this by stimulating protein synthesis through the enzyme RNA polymerase I. Protein is a basic building block of cell walls, cell structures, and enzymes that are vital to all body processes. Milk thistle's regenerative ability is essential for treating serious conditions such as chronic hepatitis, cirrhosis, and toxic fatty deposits in the liver.

