

Liver Protectant.

Used in Herbal medicine to increase bile excretion by the liver.

RxBalance™ Liv-tox stimulates toxin elimination with six herbal ingredients, each known for their liver cleansing properties. Liv-tox supports detoxification cycles (Phase I and II), up-regulates glutathione production and improves Superoxide Dismutase production. Liv-tox provides protection to hepatocytes and supports their regeneration, improves bile flow and helps modulate and protect liver enzyme integrity. It has cholorectic and anti-inflammatory effects, protects DNA and is supportive during chemotherapy.

Ingredients: Medicinal

Each capsule contains:

Milk Thistle (<i>Silybum marianum</i>) seed extract (std. to 80% silymarin, providing 120 mg)	150 mg
Artichoke (<i>Cynara scolymus</i>) leaf 4:1 extract, equivalent to 600 mg raw herb	150 mg
Turmeric (<i>Curcuma longa</i>) rhizome 25:1 extract equivalent to 2500 mg (std. to 95% curcumin)	100 mg
Schisandra (<i>Schisandra chinensis</i>) fruit 5:1 extract equivalent to 500 mg (std. to 2% schisandrins)	100 mg
Picrorhiza (<i>Picrorhiza kurroa</i>) root 4:1 extract equivalent to 200 mg (std. to 4% kutkin)	50 mg
Niruri (<i>Phyllanthus niruri</i>) herb 8:1 extract equivalent to 400 mg	50 mg

Ingredients: Non-medicinal

Hypromellose, stearic acid.

This product does not contain dairy, egg, gluten, shellfish, soy, sulfites, animal derivatives or artificial colours, flavours or preservatives.

Recommended Use

Hepatoprotectant/Liver protectant. Used in herbal medicine to increase the bile excretion by the liver (cholorectic).

Recommended Dose

Adults take 1 capsule once daily. Use for a minimum of three weeks to see beneficial effects.

Risk Information

Do not use if you are pregnant or breastfeeding, allergic to plants of the Asteraceae/Compositae/Daisy family, or if you have a bile duct obstruction. Consult a health care practitioner prior to use if you are taking antiplatelet medication or blood thinners, if you have stomach ulcers or excess stomach acid, or if you have impaired liver function, gallstones or persistent diarrhea. Consult a health care practitioner if symptoms persist or worsen. Hypersensitivity/allergy has been known to occur, in which case, discontinue use.

Interactions with Drugs/Supplements

If you are taking Cytochrome P450 2C9 (CYP2C9) substrates such as amitriptyline (Elavil), diazepam (Valium), verapamil (Calan), warfarin (Coumadin), zileuton (Zyflo), and others, Cytochrome P450 3A4 (CYP3A4) substrates, estrogens, anti-diabetes or glucuronidated drugs consult a health care practitioner prior to use.

Dosage Form Description

A vegetable capsule with a yellow powder fill.

Packaging

Available in bottles of 60 capsules.

Stability

Shelf life of three years if stored in a cool, dry place.

Ingredient Description

Milk Thistle (*Silybum marianum*) is used orally for liver disorders including toxic liver damage caused by chemicals, jaundice, chronic inflammatory liver disease, hepatic cirrhosis and chronic hepatitis. Silymarin, the active constituent, consists of four flavonolignans called silybinin (silybin), isosilybinin, silchristin (silychristin) and silidianin. When ingested, silymarin undergoes enterohepatic recirculation and has higher concentrations in liver cells.¹

Artichoke (*Cynara scolymus*) is used orally for treating liver dysfunction, dyspepsia, hyperlipidemia, preventing gallstones, lowering blood pressure and as a tonic. The active components include a mixture of polyphenols and flavonoids including caffeic acid, chlorogenic acid, cynarin, luteolin-7-O-glycoside (cynaroside), and luteolin.²

Turmeric (*Curcuma longa*) is used orally for liver and gallbladder complaints, jaundice, hepatitis, diarrhea and kidney inflammation. Its major active component is curcumin (diferuloylmethane), a yellow pigment which exhibits anti-inflammatory activity, possibly inhibiting cyclooxygenase-2 (COX-2), prostaglandins, and leukotrienes.³

Schisandra (*Schisandra chinensis*) Orally, schisandra is used as an adaptogen for increasing resistance to disease and stress, increasing energy, liver protection and energizing RNA-DNA to rebuild cells. Schisandra improves liver function by increasing hepatic glutathione, glucose-6-phosphate, and glutathione-reductase activity. It thought to be hepatoprotective by inhibiting lipid peroxidation, increasing liver glycogen production, inducing cytochrome P450 (CYP450) enzymes, and promoting hepatocyte growth.⁴

Phyllanthus (*Phyllanthus niruri*) is used orally for urinary tract infections and inflammation, kidney stones, jaundice, hepatitis B, as a diuretic, an antifatulent, liver tonic and blood purifier. It is thought to have multiple properties; antispasmodic, antiviral, bactericidal, antipyretic and diuretic. It is also thought that Phyllanthus reduces blood sugar and protects the liver.⁵

Picrorhiza (*Picrorhiza kurroa*) is used orally for jaundice, acute viral hepatitis, indigestion, constipation, fever, allergy, and asthma. Other uses include vitiligo, eczema, infection, scorpion stings, chronic diarrhea, epilepsy, malaria, and rheumatoid arthritis. There is preliminary evidence that the constituent picroside might protect against liver injury. Picroliv, a combination of picroside, kutkoside, cucurbitacin glycosides, and other unidentified constituents, also appears to have hepatoprotective activity. Picroliv seems to protect the liver from hepatotoxic agents, such as ethanol and the Amanita mushroom. This protective effect against liver damage might be due to the prevention of lipid peroxidation and generation of free radicals, decreasing the formation of reactive metabolites.⁶

Reason for Combination

The liver plays an important role in protecting the organism from potentially toxic chemical insults through its capacity to convert lipophiles into more water-soluble metabolites which can be efficiently eliminated from the body via the urine. This protective ability of the liver stems from the expression of a wide variety of xenobiotic biotransforming enzymes whose common underlying feature is their ability to catalyse the oxidation, reduction and hydrolysis (Phase I) and/or conjugation (Phase II) of functional groups on drug and chemical molecules. The broad substrate specificity, isoenzyme multiplicity and inducibility of many of these enzyme systems make them particularly well adapted to handling the vast array of different chemical structures in the environment to which we are exposed daily. However, some chemicals may also be converted to more toxic metabolites by some of these enzymes, implying that variations in the latter may be important predisposing factors for toxicity.

Milk thistle contains silibinin which is the major pharmacologically active compound of the *Silybum marianum* fruit extract silymarin. Its well-known hepatoprotective activities are mostly explained by antioxidative properties, inhibition of phosphatidylcholine synthesis or stimulation of hepatic RNA, protein synthesis and immune-response modifier.

A portion of **artichoke's** liver protective properties is thought to be attributed to its documented antioxidant actions. A 2002 study by Zapolska-Downar D. et al, focused on the antioxidant effects of artichoke extract in cultured blood vessel cells and reported that the extract demonstrated "marked protective properties against oxidative stress induced by inflammatory mediators". Artichoke's antioxidant properties were also confirmed in an earlier study that focused on human white blood cells under various induced oxidative stresses.

Turmeric's major active constituents are curcuminoids including curcumin (diferuloylmethane), a yellow pigment. It seems to have anti-inflammatory activity, possibly by inhibiting cyclooxygenase-2 (COX-2), prostaglandins, and leukotrienes. Turmeric also exhibits chemopreventive and growth inhibitory activity against several tumour cell lines. It seems to induce apoptosis in cancer cells and may inhibit angiogenesis. In addition, curcumin might have antithrombotic effects. Preliminary research suggests it might inhibit platelet-activating factors and arachidonic acid platelet aggregation, possibly by interfering with thromboxane synthesis, while other research suggests that turmeric might also have antioxidant and immunostimulatory effects.

The major active compounds in **schisandra** are lignans (schisandrin, deoxyschisandrin, gomisins, and pregomisin) found in the seeds of the fruit. Modern Chinese research suggests these lignans have a protective effect on the liver and an immuno-modulating effect. In China, crude schisandra berries, their preparations, and individual constituents are widely used for progressive hepatic degeneration due to viral hepatitis or chemical challenge-indications for which schisandra is well documented. Part of how schisandra lignans appear to protect the liver is by activating the enzymes in liver cells that produce glutathione, an important antioxidant. Other properties include the inhibition of phosphatidylcholine synthesis, stimulation of hepatic RNA, protein synthesis and immune-response modifier.

PRODUCT CODE: 403 900 - 60 Capsules

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Research Synopsis

1. **Milk Thistle (*Silybum marianum*)** Abnormal result of liver function tests and/or abnormal haematological values were observed in 49 of 200 workers exposed to toluene and/or xylene vapours for 5-20 years. Thirty of the affected workers were treated with Milk thistle for 30 days. The remaining 19 were left without treatment. Under the explanation of Legalon the liver function tests and the platelet counts significantly improved.⁷
2. **Turmeric (*Curcuma longa*)** The study investigated the effects of curcumin, a major antioxidant constituent of turmeric, on hepatic cytochrome P450 (CYP) activity in rats. Wistar rats received curcumin-containing diets (0.05, 0.5 and 5 g/kg diet) with or without injection of carbon tetrachloride (CCI(4)). The hepatic CYP content and activities of six CYP isozymes remained unchanged by curcumin treatment, except for the group treated with the extremely high dose (5 g/kg). This suggested that a daily dose of curcumin does not cause CYP-mediated interaction with co-administered drugs. Treatment with curcumin at 0.5 g/kg alleviated the CCI(4)-induced inactivation of CYPs 1A, 2B, 2C and 3A, 2C and 3A isozymes, except for CYP2E1. The lack of effect of curcumin on CYP2E1 damage might be related to suicidal radical production by CYP2E1 on the same enzyme. It is speculated that curcumin inhibited CCI(4)-induced secondary hepatic CYPs damage through its antioxidant properties. Results demonstrated that CYP isozyme inactivation in rat liver caused by CCI(4) was inhibited by curcumin. Dietary intake of curcumin may protect against CCI(4)-induced hepatic CYP inactivation via its antioxidant properties, without inducing hepatic CYPs.⁸
3. **Schisandra (*Schisandra chinensis*)** The study evaluated the potential activity of *Schisandra chinensis* in restoring hepatic drug metabolism in CCl4 damaged liver; antipyrine was employed as a probe for the possible effects of the herb on Phase I oxidative metabolism in rats. Schisandra lignan fraction (160 mg/kg) was given orally to male Sprague-Dawley rats (220-240 g) 30 min or 6 h before CCl4 intoxication (4 ml/kg, s.c.). Pretreatment with the Schisandra lignan fraction 30 min or 6 h before intoxication significantly ($P < 0.001$) improved antipyrine elimination. Moreover, normalization of SGPT, SGOT and P450 levels was observed with the two Schisandra pretreatment schedules. In conclusion, Schisandra lignans exhibited strong protective effect on Phase I oxidative metabolism in the liver damaged by CCl4.⁹

References

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2. www.naturaldatabase.com Artichoke Monograph (as of July 2006)
3. www.naturaldatabase.com Turmeric Monograph (as of July 2006)
4. www.naturaldatabase.com Schisandra Monograph (as of July 2006)
5. www.naturaldatabase.com Phyllanthus Monograph (as of July 2006)
6. www.naturaldatabase.com Picrorhiza (*Picrorhiza kurroa*) Monograph (as of Aug. 2006)
7. Szilard S, Szentgyorgyi D, Demeter I. Protective effect of Legalon in workers exposed to organic solvents. *Acta Med Hung.* 1988;45:249-56.
8. Sugiyama T, Nagata J, Yamagishi A, Endoh K, Saito M, Yamada K, Yamada S, Umegaki K. Selective protection of curcumin against carbon tetrachloride-induced inactivation of hepatic cytochrome P450 isozymes in rats. *Life Sci.* 2006 Apr 4;78(19):2188-93. Epub 2005 Nov 8.
9. Zhu M, Lin KF, Yeung RY, Li RC. Evaluation of the protective effects of *Schisandra chinensis* on Phase I drug metabolism using a CCl4 intoxication model. *J Ethnopharmacol.* 1999 Oct;67(1):61-8.

