

# Silymarin: Insights into Properties and Therapeutic Indications

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**Abstract** Silymarin is the active ingredient of milk thistle. Several studies proved that silymarin has antioxidant, anti-inflammatory and anti-cancer properties. Silymarin is widely used for treatment of hepatic and biliary disorders, renal toxicity and is recently used as adjuvant agent for treatment of cancer.

**Keywords:** silymarin, properties, indications

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## 1. Introduction

The use of medicinal plants in treating illnesses has been reported since ancestral times [1]. Silymarin is a flavonoid that has been introduced as a hepatoprotective agent. It is the most well known compound of the flavonoids due to its well defined therapeutic properties. It is extracted from the seeds and fruit of *Silybum marianum* and is a mixture of three structural components: silibinin, silydianine and silychristine. Of these three isomers, silibinin is the most active cytoprotectant [2]. Silymarin is used for the treatment of numerous liver disorders characterised by degenerative necrosis and functional impairment [3].

## 2. Pharmacokinetics

Silymarin is poorly water-soluble and is usually administered in capsules as a standard extract (70 to 80% silymarin). Peak plasma concentrations are achieved in 4 to 6 hours. Silymarin rapidly conjugates with sulfate and glucuronic acid in the liver. It is mainly excreted in the bile and, to a lesser degree, in urine [4].

## 3. Pharmacodynamics

### 3.1. Antioxidant Properties

Silymarin usually possess good antioxidant activity [5]. The water-soluble dehydrosuccinate sodium salt of silibinin is a powerful iron chelator and thus inhibits the oxidation of linoleic acid catalysed by Fe<sup>2+</sup> salts [6]. It has been reported that the protective effect of silymarin is mediated by the slowing Ca<sup>2+</sup> metabolism thus forming

inactive chelates towards hydroperoxides and inhibiting the initiation step of auto-oxidation [7].

Silymarin may inhibit lipid peroxidation by scavenging free radicals and increasing intracellular concentration of glutathione [8]. Soto et al. [9] reported that the protective effect of silymarin on pancreatic damage induced by alloxan may be due to an increase in the activity of antioxidant enzymes. Silybin has protective effect against ischemia/reperfusion injury by affecting the xanthine dehydrogenase/xanthine oxidase ratio in the rat kidney [10].

Silymarin and silibinin inhibit the absorption of toxins and prevent them from binding to the cell surface. Furthermore, silymarin and silibinin, by interacting with the lipid component of cell membranes, can influence their chemical and physical properties rendering cell membrane more resistant to lesions [11].

### 3.2. Anti-Inflammatory and Anticarcinogenic Properties

A number of studies have suggested that silymarin is an anti-inflammatory that regulates inflammatory mediators such as tumor necrosis factor, nitric oxide and interleukins [1,12]. Silymarin increases lymphocyte proliferation, interferon gamma and cytokines. Silymarin also exerts other effects, including inhibition of neutrophil migration, inhibition of synthesis of leukotrienes and prostaglandins [13].

The protective effect of silymarin against carcinogenic agents has been studied in various experimental animal models. Silymarin significantly reduces apoptosis, skin oedema, depletion of catalase activity and induction of cyclo-oxygenase activity. This provides protection against burn-induced oxidative skin injury and photocarcinogenesis. Also, silymarin was proven to inhibit nasopharyngeal carcinoma cells [14].

The molecular bases of the anti-inflammatory and anticarcinogenic effects of silymarin are not yet known; they may be due to inhibition of the transcription factor NF- $\kappa$ B, which regulates the expression of various genes involved in the inflammatory process and carcinogenesis. Also, direct targeting of MEK1/2 and RSK2 by silymarin induces cell-cycle arrest and inhibits melanoma cell growth [15].

### 3.3. Antifibrotic Effects

In response to fibrogenic influences, stellate hepatocytes proliferate and transform into myofibroblasts responsible for the deposition of collagen fibres in the liver. Silibinin reduces the proliferation of stellate cells of rats, reduces the conversion of such cells into myofibroblasts and downregulates gene expression of extracellular components responsible for fibrosis [1,3].

Furthermore, silymarin acts not only on the cell membrane, but also on the nucleus, it increases protein synthesis by stimulating RNA polymerase I and the transcription of rRNA, this is an important step in the repair of cellular injury and is essential for restoring structural proteins and enzymes damaged by toxins [16].

## 4. Therapeutic Indications

Silymarin is used for treatment of acute viral hepatitis, treatment of hepatitis induced by toxins or drugs and to reduce complications associated with chronic hepatitis, liver cirrhosis and alcohol-related liver disease [17]. Also, it may be used to prevent nephrotoxicity induced by chemotherapeutic agents such as cisplatin [18]. The acute toxicity of silymarin is very low and it is devoid of embryotoxic potential [6,19].

## 5. Conclusion

There is a strong evidence suggesting that silymarin treatment improves hepatic diseases, renal diseases and cancer. However, some of the data are contradictory. Therefore, additional molecular studies are needed to investigate the mechanisms of action for these compounds. It is known that silymarin does not possess adverse effects even at high doses. Thus, it is a natural compound that is widely used in traditional medicine and has been investigated in formal scientific studies.

## Competing Interests

The author has no competing interests.

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