

# A critical review on silymarin as hepatoprotective and newer applications

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## ABSTRACT

Silymarin is a popular antioxidant medicinal plant which is used in various traditional as well as modern diseases. It has potential health benefits which are yet unexplored. Silymarin well known for use in various skin disease, liver disease, autoimmune diseases, alcoholic liver disease and non-alcoholic fatty liver disease (NAFLD), anti-inflammatory, cytoprotective, and neuroprotective effect. Silymarin also improve behavioural pattern in various animal studies. It inhibit release of various types of inflammatory cytokines. This review focus on mainly hepatoprotective effect of silymarin and some newer application which are reported.

## 1. Introduction

Silymarin, reverse the harmful effects of solar ultraviolet radiation such as inflammation, immune responses, DNA damage, and pigmentation due to its antioxidant property.

The most frequent liver diseases caused by inflammation which have different etiologies and characteristics. Generally causes of chronic inflammatory liver diseases are excessive alcohol consumption, exposures chemicals, sedentary lifestyle, metabolic syndrome diseases, autoimmune diseases, alcoholic liver disease and non-alcoholic fatty liver disease (NAFLD). Other diseases also occur by the hepatotoxic substance which causes inflammation such as chronic biliary diseases, hereditary metabolic diseases and hepatic attacks [1]. Méndez-Sánchez et al[2] some epidemiological study estimate the prevalence of chronic liver diseases by the 2050 are approximately upto 2 million cases. Studies shoen silymarin effectively reduce liver function tests(LFT) such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST)

levels in liver diseases, and use for beneficial effect on patients[3]. Silymarin have shown effect on various disease of different organ such as kidney, lungs, skin and brain[4]. The silymarin extracted from milk thistle is known to have antioxidant, antiviral and anti-inflammatory properties .

For liver disease Silymarin (*Silybum marianum*), an extract of milk thistle, was reported for hepatoprotective effect [5,6]. Indeed, silymarin used for chronic HCV infection and cirrhosis with 33% of patients use for treatment of their disease[7]. In-vitro Silymarin reported it having anti-inflammatory and immunomodulatory properties due to inhibition of NF- $\kappa$ B (nuclear factor  $\kappa$ -light-chain-enhancer of activated B cells) [8,9]. Studies of silymarin in the HCV replicon system also suggest an effect on HCV core and NS5A expression, although at high concentrations[10]. Silymarin shows same pathways in the pathogenesis of chronic liver disease and potential treatment for chronic HCV infection.



## 2. General pharmacology

Silymarin and its constituents shows the hydrophobic-hydrophilic interface of the microsomal bilayer that affecting the

packing of the acyl chains and restoring the membrane fluidities of liver microsomes and mitochondria [10,11]. Silymarin shows membrane-bound enzymatic activities due to stabilizing effect at

membrane level. [12]. In-vitro hepatocellular plasma membrane stability increases at At high concentrations, silymarin [13].

### 2.1 Silymarin as hepatoprotective

In preclinical experimental data shows hepatoprotective effect that pretreatment with silibinin prevents or mitigates hepatic injury by toxins (i.e., ethanol, galactosamine, phalloidin, and CCl<sub>4</sub>) [14] or progression of fibrosis[14,15]. Extrapolate these observation in animal study to clinical study is quite difficult except a few cases reports, no evidence of liver disease caused by drugs or chemicals which can prevent by the silibinin. In large scale IV silibinin administration Possibly prevent the death cup (*Amanita phalloides*) intoxication. Silibinin is a specific antidote of amanitin. The effect in mushroom poisoning is explained by the stimulation of nucleolar polymerase A, inhibits lipid peroxidation and increases ribosomal protein synthesis[16]. And more silibinin is pharmacological active compound with various properties that beneficially reverse liver disease of various causes but no controlled data are available. Unfortunately, clinical efficacy well- controlled prospective studies are missing to document.for oral prepaton of silymarin is limited. Problem may solve by Improving preparations bioavailability.

#### Mechanism of action:

Silymarin's hepatoprotective effects via several mechanisms; these include:

- Antioxidation[17,18].
- Inhibition of lipid peroxidation[19].
- Stimulation of ribosomal RNA polymerase and subsequent protein synthesis, leading to enhanced hepatocyte regeneration[20].
- Enhanced liver detoxification via inhibition of phase I detoxification[21,22].
- Enhanced glucuronidation and protection from glutathione depletion[23].
- Anti-inflammatory effects, including inhibition of leukotriene and prostaglandin synthesis, Kupffer cell inhibition, mast cell stabilization, and inhibition of neutrophil migration[24,25].
- Slowing reduction of the conversion of hepatic stellate cells into myofibroblasts[26].

- It having immunomodulatory effects on the diseased liver[27,28].

### 3. Newer application

#### 1) Silybin/silymarin as chemoprotective and anticancer agents

Silymarin help to inhibit the carcinogenic effect of many chemicals due to its chemopreventive action. N-butyl-N-(4-hydroxybutyl) nitrosamine were significantly reduced in the incidence of urinary bladder neoplasms and preneoplastic lesions [29]. In azoxymethane induced in rat the Silymarin also significantly inhibited in colon cancer [30]. Silymarin inhibited by benzoyl peroxide or 12-O-tetradecanoylphorbol-13- acetate induced skin carcinogenesis [31].

#### 2) Silybin/silymarin in treatment and prevention of gastrointestinal problems

Silybin/ silymarin preparation can be used for treatment or prevention of Many gastrointestinal problems. Silybin shows mainly chemoprotectant and can induce recovery after intoxication. In alloxane induce rat model effect of alloxane which causes cell death of b-pancreatic cells and decrease of insulin secretion,causes production of Alloxane, which causes production of reactive oxygen species which produce cellular damage followed by cell death. In hyperglymic rat silymarin shows prevent a rise in both plasma glucose and pancreatic lipid peroxidation 0[32,33].

#### 3) Silybin/silymarin in skin protection

In various animal tumor models Silymarin has been shown preventive effects against photocarcinogenesis. In comparative study topically silymarin treated and non-treated application to mouse skin reduced UVB-induced tumor incidence, multiplicity, and size 34].Silybin administered topically or in the diet inhibited photocarcinogenesis in mice [35].

### 4. Conclusion

This review gives information of the silymarin as hepatoprotective and newer application. Silyamrin having activity antioxidant, skin disease and anticancer agents.

This review can be used for further research of silymarin.

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