

**Pharmacological and Pharmacognostic Activity of *Silybum marianum***

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DOI:

## Article Info:

Received 1 May 2020

Accepted 14 Jun 2020

Published 1 Aug 2020

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Herbs have been utilized for all time as the significant sources of medication. Medical plants are significant by optional metabolites, for example; *Silybum marianum*, is a remedial herb with a thousand years history of utilization. It is a blend of flavonoids, called silybin, which isn't just the major silymarin component but at the

same time is the most dynamic element of this extract, which has been affirmed in different studies.

This compound has a place with the flavonoid group known as flavonolignan. Silybin's structure comprises in two fundamental units. The first depends on a taxifolin, the second a phenylpropanoid unit, which for this situation is conyferil liquor. These two units are connected together into one structure by an oxeran ring contains mixtures (taxifolin, silychristin, silydianin, silybinin A and silybinin B).

The present study is fundamentally centered on the medicinal importance of *Silybum marianum*, its utility as a medicinal plant for the treatment of different issues of mind, cardiovascular, hepatic, kidney, and oxidative stress also, malignant growth is outstanding. As far as its medicinal properties, *Silybum* has no symptoms. In any case, it might cause mild nausea or gastrointestinal difficulties in uncommon cases. The leaves, seeds or some of the time the entire plant is utilized in medicinal preparation.

**Key words:** *Silybum marianum*, flavonolignan called silybin.

**الفعالية الدوائية والعقاقيرية لنبات الكلغان (*Silybum marianum*)**

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**الخلاصة:**

أستخدمت الأعشاب في جميع الأوقات كأهم الأدوية. وتعتبر النباتات الطبية مهمة من خلال المستقلبات الإختيارية، على سبيل المثال، *Silybum marianum*، هو عشب علاجي له تاريخ استخدام يبلغ ألف سنة. وهو مزيج من مركبات الفلافونويد، التي تسمى سيليبيين، كما أنه ليس فقط عنصر سيليمارين الرئيسي ولكنه في نفس الوقت العنصر الأكثر ديناميكية من هذا المستخلص، والذي تم تأكيده في دراسات مختلفة.

هذا المركب له مكان مع مجموعة الفلافونويد المعروفة باسم الفلافونولينان. ويتكون هيكل Silybin من وحدتين أساسيتين: الأولى تعتمد على التايوفولينات، والثانية هي وحدة فينيلبروبانويد، والتي في هذه الحالة هي سائل conyferil. وترتبط هاتان

الوحدتان معاً في هيكل واحد عن طريق حلقة أوكسيران تحتوي على خلطات (تاكسيفولين، سيليكريستين، سيليديانين، سيليبينين أوسيليبينين ب).

تركز الدراسة الحالية بشكل أساسي على الأهمية الطبية لـ *Silybum marianum* ، وفائدتها كنبات طبي لعلاج المشاكل المختلفة بدءاً من الدماغ، القلب والأوعية الدموية، الكبد، الكلى، والأكسدة وأيضا النمو الخبيث (ألورام الخبيثة). أما فيما يتعلق بخصائصه الطبية، فليس لدى *Silybum* أي أعراض جانبية، وقد يسبب (في أي حال) الغثيان الخفيف أو صعوبات الجهاز الهضمي في الحالات غير المألوفة. ويمكن استخلاص الأوراق أو البذور أو يتم استخدام النبات بأكمله في التحضير الطبي.

## Introduction

Plants are a significant source of sustenance, nourishment, flavors, fiber, shades, pharmaceuticals, Agrochemicals, insecticides. These are auxiliary mixes present in scientific categorizations; these mixes are significant for the biological cooperation's not valuable for the survival of these plants [1-3]. *Silybum marianum* (L.) Gaertn regular name is milk thistle; it is a palatable plant has a place with the Asteraceae family. Four different isomers were separated from its secondary compound silymarin (silidianini sibilinin, silibinin and sacristan) [4]. Milk thistleish-epatoprotectants for malignant growth Patients. Toleration of malignancy therapy may advance from utilizing this herb; reason is that it is blood and liver toxin

**الكلمات المفتاحية:** سيليبومماريانوم، الفلافونولينان.

clearing operators [5]. It has strong anticancer impacts against breast, tumors, ectocervical and prostate [6]. Against the ovarian disease, it improved the viability of doxorubicin and cisplatin in vitro investigation [7]. *Silybum marianum* has been utilized securely for youngsters, older and pregnant ladies [8-10]. It is utilized in cholestatic, etiologies, viral, heavy drinker and poisonous impact expelling prescriptions [11]. Since the first century milk thistle has been utilized restoratively [12,13], its flower, leaves and roots have been utilized as European eating regimens as vegetable, and its achene is utilized as an espresso. It considered as a spinach substitute. The blossom head is utilized for medication. It is utilized as a cure for Amanita mushroom toxin [14,15].



**Figur(1):Leaves, seeds of white and purple flowering varieties of *Silybum marianum* .reaserchgate.com**

## Morphological characters

Milkthistle, is a tall plant having smooth white veins, dark green leaves, thistles on the stems, and purple bloom [15,16]. It has capacity to accomplish a stature of 2 m with prickly edges leaves [17]. Single inflorescences and at the pinnacle enormous heads are situated with branches. The florets are rounded, bisexual having purple,

red or white color [18,19]. Milk thistle is generally self-pollinator [20]. Milk thistle dust grain shape is prolatewhen looks at equatorial regionand appears semi precise in polar sight [21]. The seeds have white pappus brownish in color, gleaming, taking hard skin achenes, for the most part six to eight milimolar long [22].

### Chemical Compounds

The seeds of this plant contain numerous mixes, example, apigenin, silybin, silibinin A and B, silicristin, deoxysilyncristin, dehydrosilybin, deoxysilyndianin, among other. Extract of dried seed of this plant contains up to 4% silymarin. Silymarin is a mix of flavonoids, example, silibinin A and B, silidianin, silicristin, and dihydroxysilibin<sup>[23,24]</sup>, other flavonolignans present in concentrate of this plant incorporate sylandrin, silybinom, palmitic, silyhermin, and myristic, and stearic acids, which may have hepatoprotective properties<sup>[25]</sup>. In addition, dried seeds of the plant contain up to 20% oil without therapeutic properties<sup>[26]</sup>.

Silymarin is promptly assimilated from the gastrointestinal tract and afterward arrives at its most extreme blood fixation following 2 to 4 hours. Its half-life discharge is 6 hours. 80% of this medication is discharged from the bile. Bioavailability of this medication relies upon the kind of definition<sup>[27]</sup>. Silybin is the best cancer prevention agent and hepatoprotective substance present in silymarin and its focus in bile is multiple times more than the other components<sup>[28]</sup>.

### Mechanisms of Action

Silymarin's hepatoprotective impacts are practiced by means of a few systems including antioxidation, inhibition of lipid peroxidation, improved liver detoxification through restraint of Phase I detoxification and enhanced glucuronidation, and security of glutathione depletion<sup>[29-31]</sup>. Studies have likewise demonstrated silymarin displays several anti-inflammatory impacts, including inhibition the leukotriene and prostaglandin combination, Kupffer cell

restraint, pole cell adjustment, and restraint of neutrophil migration<sup>[32]</sup>.

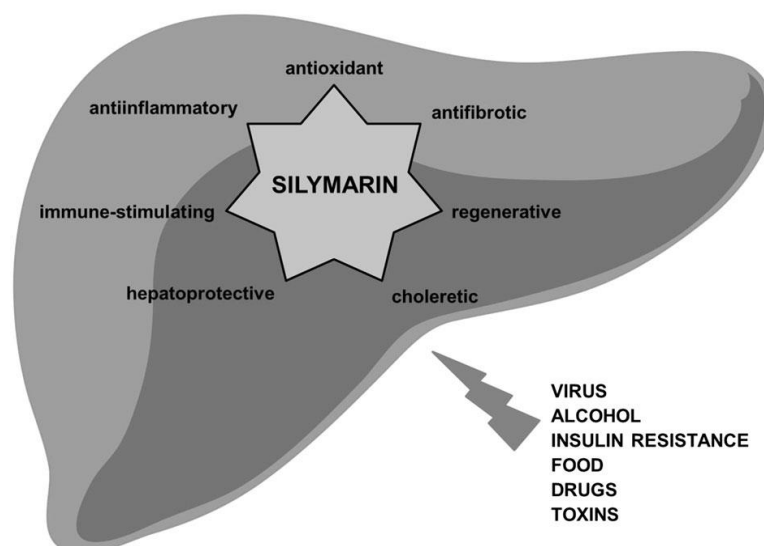
Likewise, silymarin has been shown to increment hepatocyte protein amalgamation; subsequently advancing hepatic tissue regeneration<sup>[33]</sup>. Animal studies have additionally exhibited silybin diminishes the change of hepatic stellate cells into myofibroblasts, easing back or even turning around fibrosis<sup>[34]</sup>. Clinical investigations led in Hungary likewise showed silymarin to have immune-modulatory consequences for the sick liver<sup>[35,36]</sup>.

### Pharmacokinetics

Silymarin has no water solubility, (pharmacokinetics), making tea arrangements incapable; consequently, it is typically administered orally in exemplified structure. Since assimilation of silymarin from the gastrointestinal tract is just moderate (23-47%), it is best regulated as an institutionalized extract of 70-80 percent silymarin. In animals and humans, peak plasma levels are come to in four to six hours after an oral portion. Silymarin is discharged fundamentally by means of the bile but some leeway is also accomplished by means of the kidneys<sup>[37]</sup>. The leeway half-existence of silymarin is six to eight hours<sup>[38]</sup>.

### Experimental pharmacology

Experimental studies have uncovered the different pharmacological properties of MT segments conceivably valuable for liver diseases. The antifibrotic, antioxidant regenerative, hepato-protective, choler-etic, immune-stimulating, and anti-inflammatory activities (Figure-2) make MT as a potential possibility for liver disease<sup>[39]</sup>.



**Figure (2): Different pharmacological functions of silymarin in liver diseases.**

Figure diverse pharmacological elements of silymarin in liver diseases cancer prevention agent (direct free extreme scavenger action), antifibrotic (represses the change of stellate cells in myofibroblasts), regenerative (invigorate hepatic recovery), choloretic (causes an upregulating of the bile salt fare siphon), hepatoprotective (stifle the arrival of cytokines), immune stimulating (avoids inflames some actuation), and calming (inhibition of NF- $\kappa$ B pathway)<sup>[40]</sup>.

### Anti-inflammatory and immune modulation

Silymarin applies anti-inflammatory activities and attenuates autoimmune and immune-mediated liver diseases, potentially by means of concealment of oxidative and nitrosative immune toxicity and Tlympho-cyfunction<sup>[41]</sup>.

A number of studies have indicated that silymarin applies anti-inflammatory activate through suppression of the release of cytokines for example as tumor necrotic factor- $\alpha$ (TNF $\alpha$ ), bond molecules example, Eselectin, as well as via suppression of atomic factor kappa-light chain-enhancer of actuated B cells (NF- $\kappa$ B)signaling, Nitric oxide with 50 lipoxigenase pathways<sup>[42]</sup>.

### Antifibrotic activity

Liver fibrosis is an aftereffect of hepatocyte injury lead to the initiate of Kupffer cells and hepatic stellate cells. The transformation of hepatic stellate cells into myo-fibroblasts is viewed as a significant occasion in fibro genesis. Liver fibrosis can bring about redesigning liver engineering prompting hepatic in adequacy, entrance

hypertension, and hepatic encephalopathy<sup>[43,44]</sup>.

### Pharmacology and Therapeutic Effects

Different useful impacts of *Silybum marianum* or its subsidiaries have been reported including hypolipidemic, hepato-protection and cardiovascular protection, anti-atherosclerosis activities, prevention of insulin resistance especially in cirrhotic patients, cancer, and Alzheimer prevention<sup>[45,46]</sup>.

### Liver Diseases

The employments of *Silybum marianum* hepatoprotective date back to 2000 years ago. Distinctive clinical and lab studies have likewise archived that silymarin protect the liver against toxicities resulting from various toxins such as tetrachloride, carbon acetaminophen and tetrachloromethane<sup>[47]</sup>. It has been reported that silymarin provides the hepatoprotective affected by various instruments by different mechanisms including action and scavenging free radicals, antioxidant, increment of cell glutathione concentration,

stabilization of hepatocellular membrane and stimulation of DNA polymerase<sup>[47]</sup>.

Various investigations have firmly recommended that the hepatoprotective impacts of silymarin are essentially because of its free radical scavenging property and antioxidant activity, the effect is reflected by glutathione modulation and the membrane stabilization that it produced. Actually the impact of silymarin on cellular permeability is related with alteration of membrane lipids including cholesterol and phospholipids. Silymarin additionally act other lipid compartments in the liver that may impact the take-up and discharge of lipoproteins<sup>[48]</sup>.

Information because of silymarin on triglyceride metabolism in the liver is meager. It is realized that in rodents silibinin is ready to partly antagonize the increase in total lipids triglycerides produced in the liver via carbon tetrachloride and, probably, to initiate unsaturated fat  $\beta$ -oxidation. It has likewise been recommended that silymarin may reduce triglyceride amalgamation in the liver<sup>[49]</sup>.

### Anticancer Effects

Laboratory data show that silymarin and particularly silybin produce chemo preventive consequences for epidermal malignancy cells, prostate cancer, as well as animal breast cancer. Silymarin showed cytoprotective consequences for malignant growth cells of prostate and human bosoms experienced with cancer-causing operators. Pre-immunization of malignant growth cells with silybin before introduction to silybin prompted expanded Adriamycin impact in the aversion of cell growth. Silymarin demonstrated cytoprotective effects prostate cancer and human breast cancer experienced with carcinogenic agents. Pre-immunization of malignant growth cells with silybin before presentation to silybin prompted expanded Adriamycin action the prevention of cell growth<sup>[49,50]</sup>.

It ought to be noticed that on account of the solid cancer prevention agent effects of *Silybum marianum*, there is a concern that this plant may produce cooperation in fixing lymphocyte toxicity capacity of chemotherapy medicines acting through biochemical per oxidative ways. However, silybin can quality cytotoxic cisplatin and doxorubicin synergistic associations, and there is no proof about its communication with their cytotoxicity effect<sup>[51]</sup>.

### Consumption during breastfeeding and pregnancy

*Silybum marianum* utilization during pregnancy, breastfeeding, and furthermore for youngsters is allowed. In spite of the fact that the symptoms brought about by plants in long term have not been demonstrated during pregnancy, during breastfeeding, and furthermore for children this belief is viewed as dependent on long term historical use as a nourishment. Utilization of this medication is recommended for the treatment of pruritus related with bile duct obstruction in pregnant women. Moreover, use of this herb in pregnant ladies leads to inhibited liver damage. Organization is essential to pregnant women poisons with Amanita mushroom<sup>[52]</sup>.

### Antioxidant properties

The antioxidant properties of milk thistle were assessed by studding the capacity to react with significant biological ROS or oxidant for example superoxide anion radical ( $O_2^-$ ), hydroxyl radical (OH $\cdot$ ), hypochlorous corrosive (HOCL), and hydrogenperoxide ( $H_2O_2$ )<sup>[53]</sup>.

Anti-inflammatory provocative anti-inflammatory impacts of silymarin are related to inhibition of the translation factor nuclear factor (NF- $\kappa$ B), which regulated facilitates the expression of various differentiation and development<sup>[54]</sup>.

### Anti-cancer Activity

Carcinogenesis is a multistep procedure that activated by changed articulation the transcriptional variables and proteins

included proliferation, cell cycles regulation, differentiations, apoptosis, angiogenesis, invasions and metastasis<sup>[55]</sup>. Silymarin and silybin are modulating lopsidedness between cell endurance and the apoptosis through obstruction with the expressions of cell cycle controllers and the proteins associated with apoptosis<sup>[56]</sup>. Anti-malignant growth movement of silymarin has been demonstrate in human body, skin cancer, breast cancer, androgen-subordinate and free prostate malignant growth, colon cancer, ovarian malignancy, cervical cancer, bladder cancer, hepatocellular carcinoma, and lung disease cells<sup>[55-57]</sup>.

### **Anti-diabetic Activity**

The properties of silymarin in decreasing fasting glycaemia and insulin level have supported the use as an anti-hyperglycaemia compound. The potent hypoglycaemia and anti-hyperglycaemic activities of an aqueous extract of milk thistle have also been demonstrated in experimental animal models of diabetes<sup>[58, 59]</sup>.

### **Hepatoprotective Activity**

Silymarin has been utilized for a considerable length of time as a hepatoprotectant<sup>[60]</sup>. This impact has been attributed to coordinate as well as such as being scavenger of receptive oxygen species, scavenger of phenylglyoxylicketyl radicals, chain breaking antioxidant<sup>[61]</sup>.

### **Clinical Indications**

#### **Amanita Mushroom Poisoning**

The most impressive utilization of silymarin is in the treatment of Amanita phalloides mushroom poisoning<sup>[62]</sup>. Genus Amanita is across the board in Europe and North America with a few palatable animal types being prized by mushroom gatherers. Significant numbers of the Amanita species are exceptionally lethal, and ingestion brings about extreme liver damage and passing in around 30% of cases, in animal studies, silymarin given within 10 minutes

after amanita toxin ingestion completely counteracted the toxic effect and whenever allowed inside 24 hours of poison ingestion silymarin forestalled demise and incredibly decreased liver damage<sup>[63]</sup>.

### **Hepatitis**

Studies have indicated silymarin to be successful in the treatment of both acute and chronic hepatitis. In acute viral hepatitis, organization of silymarin abbreviated treatment time and brought down serum bilirubin, AST, and ALT, in patients with chronic hepatitis, 420 mg silymarin per day for every day for a half year yielded improved serum liver enzymes<sup>[64]</sup>.

### **Alcoholic Liver Disease and Cirrhosis**

Studies led in Austria and Hungary have shown silymarin organization brought about a normalization of serum liver enzymes' and absolute bilirubin levels in patients with alcoholic liver disease, in addition to improve liver tissue histology.<sup>27</sup> In patients with cirrhosis a long-term about 41 months administration of silymarin at 420 mg for each day brought about a critical increment in survival compared with the fake treatment group<sup>[65,66]</sup>.

### **Hypercholesterolemia**

An animal studies covered silymarin given to rodents with diet-incited hypercholesterolemia exhibited an anticholesterolemic impact like probucol, with an expansion in HDL cholesterol and lessening altogether and billiard cholesterol<sup>[67-69]</sup>.

### **Psoriasis**

The estimation of silymarin in the treatment of psoriasis might be because of its capacity to improve endotoxin removal by the liver, inhibit cAMP phosphodiesterase, and inhibit leukotrien synthesis. Abnormally elevated levels of cAMP and leukotrienes have been seen in patients with psoriasis and standardization of these levels' maid improves the condition<sup>[70]</sup>.

**Dosage/Toxicity**

*Silybum marianum* normally given a standardized concentrate (70-80% silymarin) in encapsulated structure, 100-300 mg multiple times day by day being the run of the mill grown-up portion. Both animal and human examinations have indicated silymarin to be non-toxic. At high portions (>1500 mg every day) laxative effect is possible due to increased bile emission and flow. Mild allergic reactions susceptible responses have additionally been noted yet were not genuine<sup>[71]</sup>.

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