

## ***SILYBUM MARIANUM*: A PLANT OF HIGH MEDICINAL IMPORTANCE-A REVIEW**

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### **ABSTRACT**

The present review is basically focused on the medicinal importance of *Silybum marianum*. Its utility as a medicinal plant for the treatment of various disorders of brain, cardiac, hepatic, kidney, oxidative stress and cancer is well known. It exists as a dangerous agricultural weed species. But it is manageable. In terms of its medicinal properties, *Silybum* has no side effects. However, it may cause mild nausea or gastrointestinal troubles in rare cases. Several drugs containing *Silybum* contents in one or the other form/combinations are available in the market. It is distributed throughout the world. In India, it is found along roadsides and barren lands. Leaves, seeds or sometimes the whole plant is used in one or the other medicinal preparation. Detailed and conscientious investigations are wanted to promote the cultivation of this medicinally important plant species. *Silybum marianum* is an exciting medicinal plant species that demand more scientific studies so that it can be fully exploited for its medicinal properties and other economic aspects.

Article Received on  
10 March 2012,

Revised on 25 March 2012,

Accepted on 2 April 2012

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**Keywords:** *Silybum marianum*; Medicinal importance; Human health troubles; Animal diseases; Treatment

**Running head:** Medicinal value of *Silybum marianum*

## INTRODUCTION

*Silybum marianum* (L.) Gaertn. was previously known as *Carduus marianus* and belongs to a family Asteraceae. It is an herbaceous plant and possesses certain specific medicinal properties and can also acts as a host for some pathogens. The plant is easy to identify due to the presence of white veins on the leaves (**Figure 1, 2**). The purple colour flowers are borne at the tip of the branch (**Figure 3**). The seeds are black to dark brown in colour and bear white silky pappus (**Figures 4, 5, 6**). *Silybum marianum* has been used to treat certain health problems, such as stomach, liver and gall bladder disorders etc. Different plant parts have been used from the last 2000 years in the preparations of various traditional medicines. The most important use of this medicinal plant is its liver protecting property which dates back to early Greek references. In 18<sup>th</sup> century, it was recommended for plague and congestive liver and spleen treatments<sup>16</sup>. Since 20<sup>th</sup> century, it has been used for the treatment of diseases like liver cirrhosis, jaundice, hepatitis and liver poisoning. In addition to these, it has also been used to stimulate breast-milk production in nursing mothers and in the treatment of patients suffering from depression. The major medicinal activities of *Silybum* are anticancer, antidepressant, antioxidant, cardio protective, demulcent, digestive tonic, hepatoprotective, hepatoregenerative, immunostimulatory and as a neuroprotective<sup>37</sup>. *Silybum marianum* is one of the well accepted medicinal plants and Silymarin is the active principle studied recently. Many sole and combined products of this species are now available in the market. Recent advancements in molecular biology have expedited the process of extraction and identification of active principle. Research is under way to find out the curative compounds so that these can be used in the manufacturing of most effective, cheaper and easily available medicines.



**Figure 1**



**Figure 2**

**Figure 3****Figure 4****Figure 5****Figure 6**

### MEDICINAL IMPORTANCE

Several historical evidences highlighted its medicinal properties. These are like: Alzheimer's disease treatment, anticarcinogenic, anticirrhotic, antidepressant, antidote to mushroom poisoning, as a galactagogue, as an emetic, control of food and seasonal allergies, cough, dyspepsia, eczema, elimination of abscesses, gallbladder disorder, gastrointestinal problems, hypocholesterolaemic, immunity enhancement, kidney disorders, liver disorders, lung ailments, migraine, motion sickness, psoriasis, skin and spleen disorders, skin cancer, sweat-inducing, to cure constipation, to cure menstrual problems, tonic and diuretic, treating infections *etc.*<sup>16</sup> Some of its key medicinal properties are as follows.



## ANTI-CANCER

The incident rate of cancer is half in the developing countries as compared to the developed irrespective of sex. Cancer survival is poorer in the developing world which may be due to late diagnose or limited assess of proper treatment. However, cancer burden can be controlled by making the people aware about the hazardous effects of tobacco and other cancer causing agents, immediate diagnose of any health related troubles and its proper treatment, by promoting physical activities and taking balanced and high nutritional value diet<sup>28</sup>. Now a day's, Milk thistle is being used in cancer research for treatment purposes. Since ancient times it has been used in detoxification and cleansing of body. It has also been used in prevention and treatment of hepatotoxicity during and after chemotherapy. Studies are underway to investigate its role as chemo preventive agent as well as in the treatment of cancer. *Silybum marianum* possess anti-inflammatory and anti-metastatic activities. Silibinin, one of the major constituent of Silymarin check the cytotoxicity induced by chemotherapy and radiotherapy<sup>23, 40</sup>. The Radiodermatitis affects doctors and healthcare professionals who diagnose and treat the problem by applying X-rays to the patients. However, some patients taking this therapy also suffer from this disease. For minimising these effects, several ointments are available but sometimes they further aggravate the problem. However, *Silybum marianum* extract composition is reducing the side effects of radiodermatitis to a great extent. Naturally occurring polyphenolic antioxidants are recognized as one of the most effective classes of cancer preventive agents<sup>3,31</sup>.

Oxidative stress is one of the main contributors towards skin carcinogenesis. Silymarin, a natural polyphenolic flavonoid antioxidant, acts against skin cancer<sup>43</sup>. Bhatia *et al.*<sup>10</sup> compared the anticarcinogenic activity of Silymarin and one of its major constituent, silibinin against prostate, breast, and cervical human carcinoma cells. The anticarcinogenic activity of Silymarin is mainly because of its chief constituent-silibinin. It has been suggested that Silymarin protects the genome, stabilize mast cells and decrease the activity of tumour promoters<sup>22</sup>. Since many antioxidants are known to inhibit the tumour promotion, studies have been conducted to understand the inhibitory effect of Silymarin. The results so obtained have suggested that Silymarin is a potent anti-tumour agent and can be used in the restructuring of large number of tumour promoters<sup>4</sup>.

Therefore Silymarin along with other chemopreventive agents have become the focus of emerging area of research interest in cancer treatment<sup>32</sup>. Further Silymarin released the

harmful effects of chemotherapy. Since Milk thistle is cardioprotective, it can also eliminate the long-term hepatic and cardiovascular effects of cancer treatment on human tissues. Studies are in progress to use it as a chemo preventive agent. The researchers may develop certain mechanisms to treat cancer directly as Silymarin is known to be an anti-metastatic<sup>40</sup>. *Silybum marianum* has the potential to be an ideal cancer preventive agent as it has no toxic effects, high efficacy, known mode of action, low cost and above all the human acceptability. In certain developed countries, doses of *Silybum* are available in the market. But in developing countries like India, research is going on for its commercial and pharmaceutical utilisation.

### ANTIDIABETIC POTENTIAL

The hypoglycaemic effect of the aqueous seed extracts of *Fraxinus excelsior* and aqueous aerial part extracts of *Silybum marianum* was studied in normal and streptozotocin diabetic rats. The aqueous extracts of *Fraxinus excelsior* seeds and *Silybum marianum* aerial parts found to be the potent hypoglycaemic agents in normal as well as diabetic rats without altering the secretion of insulin. This has authenticated the traditional use of these plant species against diabetes. However, exact mechanism of action and active constituents along with toxicological effects, if any is still wanted<sup>34</sup>.

A benefit in the form of an improved glycemic profile has been observed in the patients treated with Silymarin. But this complementary therapy further needs more and detailed investigations<sup>26</sup>. At the same time another study was carried out to check the effects of anti-apoptotic and anti-inflammatory properties of Milk Thistle in treatment of steatohepatitis (fatty liver) in rats. Histopathological examinations have revealed that crude extract of *Silybum marianum* abated the severity of non-alcoholic steatohepatitis (NASH). It was suggested that this activity of the crude extract was mainly because of its antioxidant and anti-inflammatory properties<sup>5</sup>.

Aliabadi *et al.*<sup>6</sup> studies the effect of *Silybum marianum* in the treatment of wounds of diabetic induced rats. The Silymarin ointment treated rats had shown reduced wound size as compared to the other group of rats. Their finding suggests that ointment containing Silymarin was effective in the treatment of diabetic rats. However, further detailed phytochemical analysis is required to investigate the actual active compound responsible for this action.

## ANTIDOTE TO MUSHROOM POISONING

The most poisonous mushroom is *Amanita phalloides* (Death cap) which is fatal for human beings. Amanitin and Phalloidin are the two powerful hepatotoxins present in this species of mushroom. Silymarin can act as an antidote to this mushroom poisoning. Silymarin, in combination with benzyl penicillin, prove quite effective against mushroom poisoning<sup>38</sup>. Silymarin inhibits the entry of  $\alpha$ -amanitin (the most toxic form of amatoxin present in *Amanita phalloides*) into the blood by combating its transport system. It also blocks the entry of amatoxin into the hepatocytes<sup>21</sup>. If it is given within 10 minutes after the toxin intake, it completely neutralizes the toxin. However, its curative potential is negligible if given after 30 minutes<sup>18</sup>.

## ANTI-HEPATOTOXIC

Now a days consumption of alcohol is becoming a societal problem. It may cause health related problems in human being. Certain studies performed on rats have shown that the injection of milk thistle protect the rats foetus from the detrimental effects of ethanol being given to them. If ethanol, diet of the progeny of pregnant rats is supplemented with Silymarin then they perform better and develop improved memories than control animals<sup>12</sup>. When the pregnant patients are unable to avoid alcohol, then to protect their unborn foetus from side effects of alcohol, Silymarin is quite useful. This herb should not be promoted for relieving the patients from alcohol abuse. It only mitigates some of the damages caused by the alcohol. However, even this achievement has shown new pathways to treat alcoholic patients.

The combined administration of both garlic and Silymarin extracts has been proved more beneficial than individual extract administration in NDEA-induced hepatotoxic rats. This has resulted in the suppression of the induction of hepatoprototoxicity by free radical scavenging. This shows that these plant extracts can successfully be used as hepatoprotective agents<sup>42</sup>. Silymarin and its flavonolignans is the compound of *Silybum marianum* and have cytoprotective activity. During investigation it was found that the different concentration of protective agents has different effect on toxic stimuli. These protective agents have ability to quench free radicals that are produced during infections and are harmful to the hepatocytes<sup>20</sup>.

## ANTI-INFLAMMATORY

*Silybum marianum* is a very effective anti-inflammatory agent. Secondary products of Silymarin produce anti-inflammatory activity in the body tissues. These reports are based on

preclinical studies, however the detailed analysis may provide some astonishing results related to the impact of Silymarin. In lower doses, Silymarin suppresses the thrombocytes functioning in mice but higher doses of Silymarin can stimulate the inflammatory processes in body<sup>29</sup>. Silymarin obtained from the fruits of *Silybum marianum* is a mixture of flavonolignans like silybin, silydianin and silychristin. It was evaluated for its anti-inflammatory and antiarthritic activities against inflammation (induced through papaya latex) and arthritis (induced through mycobacterial adjuvant) in rats. Results have shown significant anti-inflammatory and antiarthritic activities through the inhibition of 5-lipoxygenase<sup>25</sup>. The oral administration of Silymarin in the form of tablets or capsules can reduce the carrageenan-induced paw oedema in rats and it can also reduce inflammation of mouse ear that has been induced due to harmful toxins. Hence, *Silybum marianum* is very much comparable to indomethacin<sup>17</sup>.

All these studies proved that milk thistle has an anti-inflammatory activity. However, there are many other proved anti-inflammatory species such as turmeric (*Curcuma longa*). Milk thistle cannot be recommended as a general anti-inflammatory agent but can be used as an alternative medicine for hepatic inflammation. However, there are some practitioners who prefer to use this herb consistently to cure the inflammation of the joints, particularly in the case of wrists<sup>36</sup>. A study was conducted on albino rats to evaluate the anti-inflammatory activity of *Silybum marianum*. Methanolic extracts of the leaf and leaf callus have shown maximum inhibition of rat paw oedema. This happened because of the presence of excessive secondary metabolites in the leaf callus extracts as compared to the natural leaf. However, both the extracts have shown anti-inflammatory activity<sup>7</sup>.

## CONSTITUENT OF COSMETICS

The Silymarin is used in cosmetics as an antioxidant in different body creams and lotions to protect the body from various skin infections. According to Malhotra and Singh<sup>35</sup>, besides its application in pharmaceutical, agricultural and food industry, *Silybum marianum* has been used in various cosmetic products. Silymarin obtained from the Milk Thistle has been used as herbal constituents of photoprotective agents. Research is underway to explore more herbal constituents as photoprotective agents. Researchers are looking for new alternative, safe, economical and more effective herbal photoprotective cosmetic formulations<sup>14</sup>. Further investigations are still awaited to determine the effects of long term use of Silymarin containing products as photoprotectant.

## HEPATOPROTECTIVE

Silymarin extracted from the *Silybum marianum* is the most widely prescribed to patients suffering from liver diseases. It was proved to be highly beneficial for the patients of liver cirrhosis resulted from the excessive use of alcohol. The Silymarin has a good safety record but there are some reports establishing that it causes gastrointestinal disturbances and skin allergies<sup>9</sup>. Milk thistle is a potential protective agent against liver diseases. Its mechanism of action is not fully known. It has been suggested that it competes with toxins for hepatocyte binding and penetration. Basic clinical trials indicated that milk thistle is beneficial for healthier patients with alcoholic cirrhosis. However, detailed experimental studies are required to draw any solid conclusion<sup>11</sup>.

Milk thistle was taken as dietary supplement by the patients suffering from chronic liver diseases. This treatment was found to be safe and tolerable. But the experimental studies conducted on patients suffering from chronic liver diseases using this plant species were unable to reduce mortality, improve liver histology or biochemical markers of liver function<sup>27</sup>. According to Abascal and Yarnell<sup>1</sup> many studies have suggested the strong and beneficial nature of Silymarin. Looking at the safety aspect, clinicians are advising its use irrespective of lack of clinical studies. This plant species can be used as food, as a tea and in the form of other preparations for addressing nonspecific diseases.

The seeds and fruits extract of *Silybum marianum* has been used as herbal medicines for the treatment of liver diseases<sup>19</sup>. *Silybum marianum* and its derivatives protects from toxins and liver cirrhosis. It has given promising results but the available data and experimentations were found insufficient (improper sample size, dose standardisation, insufficient information by the patient, inconsistency of the treated population etc.) to recommend this plant to be used in the treatment of alcoholic liver disease patients<sup>8, 39</sup>. Different formulations of Silymarin are prepared by encapsulating them in lipid microspheres. The potential of Silymarin was found to be increased in lipid microspheres. This shows that these can be used as carriers for efficient administration. The delivery of Silymarin by this method further pronounces the effect of hepatoprotective drug molecules<sup>2</sup>. The flavonoid compounds of *Silybum marianum* have been reported to be a potent hepatoprotective in nature. The effect of polyphenolic extracts of *Silybum marianum* and *Cichorium intybus* was tested on hepatotoxicity induced rats. Their finding proves the hepatoprotectivity of these extracts against hepatic cell injury induced by Thioacetamide<sup>33</sup>.



## TREATING CERTAIN WOMEN PROBLEMS

Silymarin is considered as a wonder drug for women. Several studies have been conducted to understand the effect of Silymarin in curing female problems. The fruits of *Silybum marianum* have been used by the nursing mothers to increase the milk production. But its mode of action is not clear. These findings suggest that Silymarin can be considered a good candidate to overcome the lactation deficiency<sup>13</sup>. After giving treatment for specific days, it increased the level of prolactin in the serum, considerably. It also helps in treating menstrual disorders and relieves the pain of menstrual cycle. In this way, it has gained popularity and females prefer to consume it orally in the form of capsules. It also acts as an anti ageing constituent in lotions and creams<sup>30</sup>.

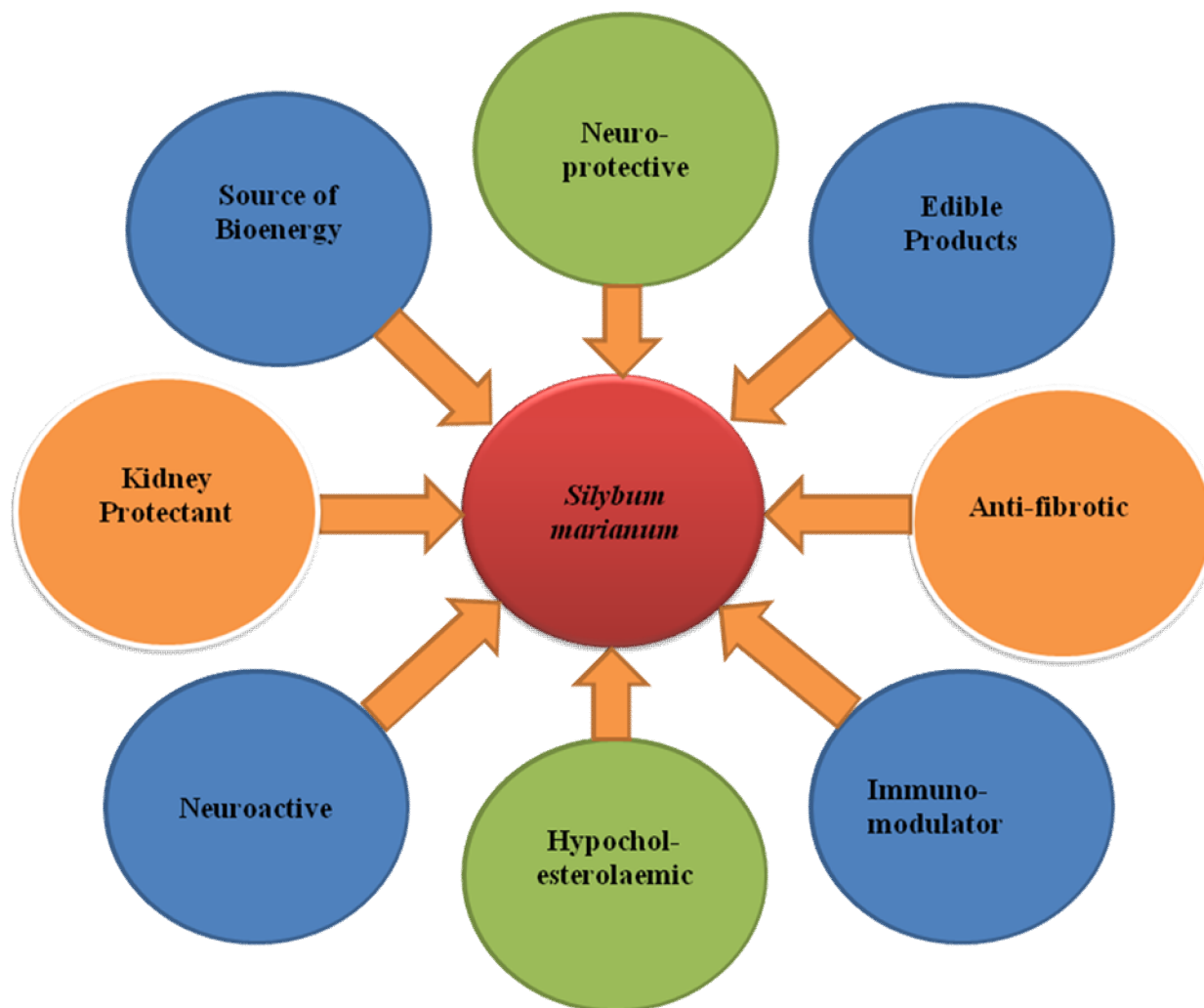
## VETERINARY MEDICINES

Milk Thistle seed cakes were added to the chick feed for fattening and to increase their body weight. Silymarin promoted body weight and also increased the hatchability in chickens and turkeys. Silymarin reduces the lipid contents and increases the glycogen content thereby acting as hepatoprotective agent<sup>44</sup>.

Schiavone *et al.*<sup>41</sup> studied the effect of fruit extract on the performance and quality of Broiler chickens. The effect of treatment on growth performance changes was insignificant. However, Silymarin can improve the meat quality. It has not shown any hepatoprotective effect but muscles' resistance to oxidative stress was enhanced. Silymarin extract was investigated for its hepatoprotective activity in white carneaux pigeons (*Columba livia*) challenged with B1 aflatoxin. Histopathology and hepatobiliary scintigraphy studies have not shown any hepatoprotective effects of Silymarin extract. However, the intake of aflatoxin resulted in hepatic inflammation, necrosis, biliary-duct hyperplasia, and lymphocyte infiltration<sup>24</sup>.

The ruminants sometimes ingests the sawfly larvae (*Arge pullata*) while grazing in the fields which causes hepatotoxicity. A compound isolated from *Silybum marianum* have been proved favourable in the treatment of hepatotoxicosis caused by sawfly larvae in ruminants<sup>45</sup>. Silymarin was also used in the treatment of *Giardia* parasitosis in dogs where the use of antibiotic, metronidazol causes hepatic disorders. The dogs treated with Silymarin had shown normal level of serum indicators of liver inflammation as compared with the positive control group in which these indicators has significantly increased which proved the importance of

Silymarin in curing liver diseases<sup>15</sup>. Some other medicinal properties of this species are shown in **Figure 7**.



**Figure 7**

## CONCLUSION

After going through various studies concerning the medicinal importance of *Silybum marianum*, certain facts have become quite clear. *Silybum marianum* has proved to be a species of great medicinal importance for the treatment of several diseases and Silymarin as a favored drug. Since it is a plant of high economic rank, it has opened several new research avenues. Its cultivation should be encouraged in order to derive maximum health benefits. Biotechnology techniques can play a better role in the development of high yielding varieties. Proper marketing of crop and its products is wanted to increase their availability. Silymarin is insoluble in water and usually administered in the form of capsules. The studies have revealed that absorption of silybinin is low when given orally. So there is a need to find some alternate way to increase its absorption in the body. Milk thistle is considered relatively safe and without any serious side effects. But sometimes minor gastrointestinal upset, laxative

effects and allergic reactions have been reported. More clinical trials involving meticulous methodology should be conducted using standardized and well defined products and dosages in order to unveil the potential of this plant species against various diseases.

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