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Review

A Review on Ethnopharmacology of *Silybum marianum*

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Abstract

Herbs have been used from ancient times as they are the major source of traditional medicine which are safer than synthetic medicines. *Silybum marianum* is one of the plants from the Asteraceae family that are usually referred to as milk thistle. The local names for *S. marianum* in India include Doodh patra (Hindi), Ratrinta (Telugu). It is indigenous to Southern Europe, Anatolia, Southern Russia, and Northern Africa. Up to now, more than 20 types of flavonolignan components have been isolated from *Silybum marianum*. The primary active ingredient in plant seeds is silymarin, which is the most widely used herbal supplement in the US and may be found in extracts, powders, and capsules. Taxifolin with a number of flavonolignans, including silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, and silydianin, combine to form silymarin which have been extensively studied because they have a variety of pharmacological properties including Anti-inflammatory, Anti-cancer, Antioxidant, and Hepatoprotective effects. Additionally, the plant is used to treat uterine diseases and acts as a galactagogue, which is an agent that causes milk secretion. This review provides a comprehensive overview of the plant's botany, phytochemistry, pharmacological activities and therapeutic uses.

Key words: *Silybum marianum*, milk thistle, silymarin, hepatoprotective.

INTRODUCTION

The herbaceous plant *Silybum marianum* has several distinct medicinal properties. Various plant parts have been used for the past two thousand years (1). This plant is widely recognized as a therapeutic herb. It is currently being recognized and extracted by using molecular biology (2). The leaves were widely utilized as cattle and horse feed in certain areas of England and Scotland. In some places with rocky or sandy soils, it is cultivated as a decorative plant in gardens (3,4). It was brought to most of Europe, Asia, North and South America, and Southern Australia as a crop (5). The plant is widely distributed around the world, existing in both wild populations and as a crop that is usually grown for its silymarin (6).

From ancient times, milk thistle has been utilized to prevent liver damage as well as to treat a diversity of gall bladder conditions, together with cirrhosis, hepatitis and jaundice (7). The US Food and Drug Administration (FDA) has authorized silybin as a phytomedicine for the treatment of liver disease. Pharmacological reports show that silymarin formulations are safe for human use since, even at greater doses,

there is no toxicity. However, there may be uncertain gastrointestinal and allergy problems. Before 10th century AD, the foremost official medical text in China included a description of the medicinal use of S. marianum in the treatment of cardiovascular diseases (8). According to experimental studies, milk thistle includes silymarin chemicals that inhibit the capecitabin-induced hand-foot syndrome, have anticancer properties, slow the proliferation of tumours cells, and lessen the negative effects of chemotherapy. This substance is applied topically to treat skin tumours and prevent UV-induced skin cancer. It also showed immunomodulation and early wound healing property (9).

Fig 1: *Silybum marianum* plant

Synonyms: Cardus marianum, Marian thistle, Variegated thistle, Venus's thistle, Christ's thistle.

Table 1: Classification of *Silybum marianum*

Rank	Scientific Name & Common Name
Kingdom	Plantae - Plants
Subkingdom	Tracheobionta - Vascular plants
Super division	Spermtophyta – Seed plants
Division	Magnoliophyta – Flowering plants
Class	Magnoliopsida – Dicotyledons
Subclass	Asteridae
Order	Asterales
Family	Asteraceae Bercht & J. Presl – Aster family
Genus	Silybum Adans. – milk thistle
Species	*Silybum marianum*- blessed milk thistle

Biological source: Milk thistle, also known as *Silybum marianum*, belongs to the Asteraceae family. It has been used for about two centuries. The plant is inherent to Australia, Southern Europe, North Africa, North and South America, and some areas of Asia. In Europe, it is commonly used as a vegetable in salads (10).

Parts used: Seeds, leaves, stem and fruits.

Distribution and habitat: Milk thistle is indigenous to the Mediterranean basin, including southern Europe, Southeast Asia, and northern Africa, but has also been cultivated in other continents. Milk thistle seeds have been used for medical purposes for over 2000 years, particularly to treat liver disorders. The plant is currently found worldwide both in wild populations and as a crop. It is typically farmed to extract silymarin. Milk thistle, often known as a ruderal species, thrives in disturbed and fruitful environments (11).

Macroscopical characters

Plant height: *S. marianum* grows to a maximum height of 2 meters, its typical height is only approximately 1.5 meters (12).

Leaves: The leaves of the milk thistle can spread an extreme length of 75 cm and a maximum width of 30 cm. They are multi-coloured and sensitive. The lower part of the leaves is furry, whereas the superior side is smooth. The leaves' veins are a creamy white colour (13).

Stem: The stem of milk thistle is 40–200 cm tall, upright, branching, glorious or somewhat downy in the upper portion of the plant.

Seed: The achene is heavy, flat, smooth, and shiny. Its colour ranges from black to brown, with a white, silky pappus and an oily, cocoa-like taste**.**

Flowers: The flower heads of purple thistles form at the tips of the stems. They are enclosed in a sticking out spiny involucre and range in diameter from 0.8 to 2.5 inches (2 to 6.4 cm) at the base. blossoms from April to July.

Fruit: The fruit consists of brown and black seeds that are roughly 0.3 inches (0.85 cm) long, slightly flattened, and have a bristle ring at the tip.

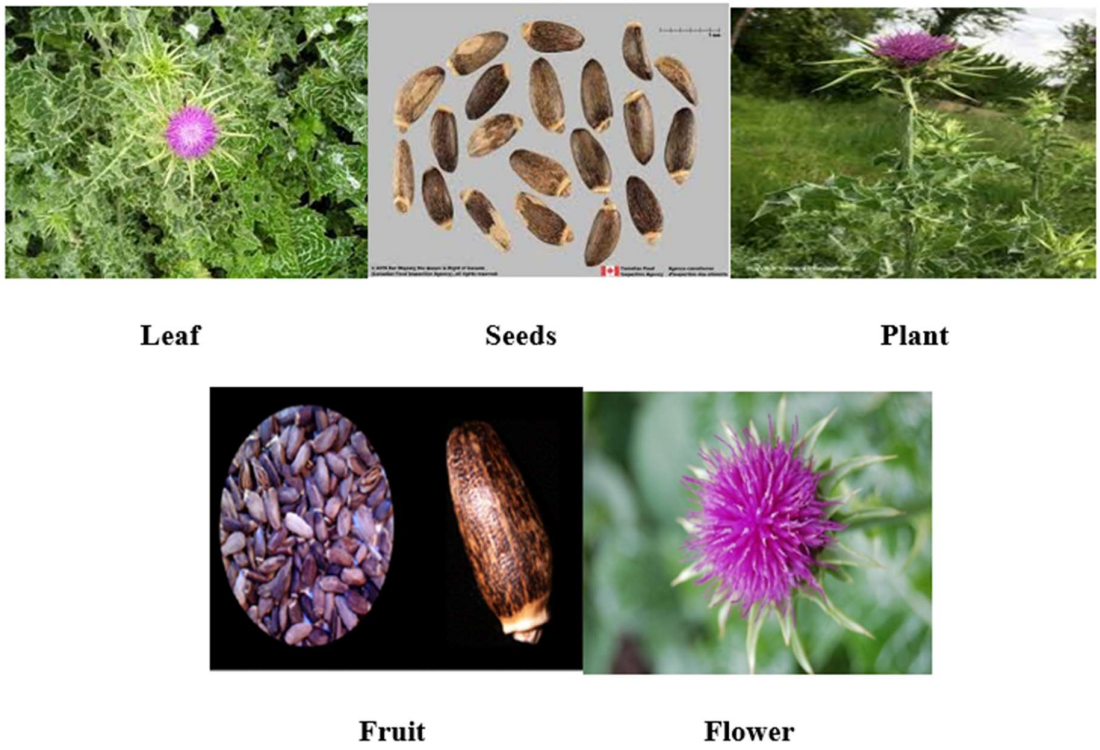

Fig 2: ***Morphology of Silybum marianum***

Growing period

Depending on the environment, milk thistle develops as an annual or biennial herb in the winter. Germination takes place in the spring and autumn. Light and temperature conditions have been found to have an impact on the germination of milk thistle seeds (14). The seeds can be planted and kept alive for up to nine years. After the growth of seedlings, milk thistle overwinters in a rosette, with an increase in the number of basal leaves occurring simultaneously. Low temperatures stimulate milk thistle to go into flowering in late winter or early spring. April through May is when Flowers takes place. July is when the achenes, or fruits, are at their ripest. The entire milk thistle growth period extended 125–140 days, which could be further subdivided into the following stages: seedling (15–20 days), vegetative (containing two stages: rosette stage and stem elongation (45–60 days), flowering, fruit-bearing, and withering. Bloom characteristically five days inside a head. After roughly 17 days, ripe fruits were released (15).

Chemical constituents

The extract having lipophilic properties from milk thistle seeds (achenes) commonly as silymarin, is the active component of the herb. which is an isomeric combination of distinct flavonoid complexes termed as flavonolignans that makes up 1.5–3% of the fruit's dry weight. In silymarin, silybin, silychristin isosilychristin, silydianin, and silimonin are the main constituents of this group. Aside from flavonolignans, the chemical composition of milk thistle fruit also includes 5,7-dihydroxy chromone, dehydroconiferyl alcohol, fixed oil (65%

linoleic acid; 30% oleic acid; 9% palmitic acid), tocopherol, sterols (cholesterol, campesterol, stigmasterol, and sitosterol), sugars (arabinose, rhamnose, xylose, and glucose), and proteins. The key constituent of the extract silybin, has the highest concentration and makes up between 50 and 70 percent of the extract, as several studies have demonstrated (16). The silymarin range of 20–40% is represented by the silybin concentrations commonly found in common medicinal formulations. Silybin has potent antioxidant qualities in addition to its hepatoprotective effects. It also modifies a number of cell-signaling pathways, which lowers pro-inflammatory mediators. Additionally, being researched is silybin's potential as a chemo preventive and anticancer agent. Previous studies have shown that silybin can inhibit serine proteases that are involved in blood coagulation and lessen blood platelets' reactivity to physiological agonists (17).

Therapeutic uses

S. marianum is known to be a safe plant. In Sardinia and Spain, different portions are eaten, such as young heads and stems. Traditionally, milk thistle has been consumed boiled and fried or utilized in salads as a fresh vegetable throughout Spain (18). Milk thistle's numerous physiological properties make it useful for a variety of medical uses. Studies have demonstrated that silymarin, which is derived from milk thistle fruits, can help cleanse and detoxify the liver and support the regeneration of damaged cells by preventing the degeneration of healthy liver cells.

A number of the active ingredients in milk thistle, such as silymarin, silybin, and others, have several potential hepatoprotective effects, such as anti-inflammatory, antioxidant, toxin-blocking, improved protein synthesis, and anti-fibrotic properties (19).

Adverse effects

When used orally, milk thistle extract is likely safe for most of the people. In some people often causes.

- Diarrhoea
- Nausea
- Loss of appetite

Pharmacological importance

Hepatoprotective activity

Since the first century, milk thistle seeds have been used to protect the liver. A key component in hepatoprotection is antioxidant activity. Liver cells in both humans and animals are protected against numerous hepatotoxins by silymarin. Certain mushrooms, such as Amanita phalloides, the death cup fungus, and A. virus, contain two toxins called phalloidin and α-amanatine, which harm and kill the liver by destroying the hepatocyte cell membrane and preventing the formation of hepatic proteins. Silymarin increases the ability of liver cells to regenerate by blocking the binding sites of the toxin, so successfully preventing both of these effects. It was discovered that silibinin, when given intravenously within 24 h of consuming mushrooms, provides an efficient defense against liver injury (20).

Additionally, silymarin provides liver protection against erythromycin estolate, amitriptyline, nortriptyline, tertbutyl hydroperoxide, and tetracycline, d-galactosamine, and thallium-induced liver damage. It reduces liver damage brought on by long-term butyrophenone or phenothiazine treatment. Silibinin significantly decreases liver damage brought on by concanavalin A. Furthermore, it offers hepatoprotection against carbon tetrachloride, acetaminophen, thioacetamide, halothane, and phalloidin poisoning. Also, it protects the liver from radiation, iron excess, and ischemic damage (21).

Several liver diseases, especially chronic liver disorders, that are characterized by degenerative necrosis and functional impairment are treated with silymarin. Silymarin is recommended by the German Commission E for the treatment of liver conditions such as chemically caused hepatitis, alcoholic cirrhosis, and hepatitis A. Cirrhosis or alcoholic liver disease: Free radical production during ethanol metabolism causes oxidative stress in the liver. Silymarin's antioxidant and hepatoprotective properties effectively fight alcoholic cirrhosis by bringing the liver's biochemical parameters back to normal. Silymarin also helps people with active cirrhosis with their cytolysis. In decompensated cirrhosis, silymarin usage is not recommended (22).

Liver fibrosis

Hepatic brain damage, portal hypotension, and hepatic insufficiency can all be caused by the modification of the liver's morphology. The primary process in fibrogenesis is thought to be the transformation of hepatic stellate cells into myofibroblasts. In patients with liver fibrosis who exhibit antifibrotic potential, silymarin therapy significantly suppresses this process.

Liver tissue regeneration

By boosting protein synthesis in the damaged liver, silymarin promotes liver tissue regeneration. Silibinin significantly increases the production of ribosomes, DNA, and proteins in both in vitro and in vivo trials

conducted in the liver of rats from which a portion of the organ (liver) was eliminated. It's interesting to note that silibinin only causes an increase in protein synthesis in damaged livers-not in healthy ones.

Anti-cancer activity

Silibin, the main component of silymarin, is primarily responsible for its anticarcinogenic properties.According t o certain theories, silymarin stabilizes mast cells, protects the genome, and lowers the activity of tumor promoter s.Studies have been carried out to study Silymarin's inhibitory effect because several antioxidants are known to prevent the promotion of tumors.The acquired results show that silymarin is a powerful antitumour drug that has the potential to alter a significant number of tumour promoters (23).

Milk thistle can also prevent the long-term hepatic and cardiovascular effects of cancer treatment on human tissues because it is a cardioprotective herb. Research on its potential as a chemo preventive agent is underway. Silymarin has been shown to be an anti-metastatic, therefore the researchers may create specific ways to treat cancer directly. Because *Silybum marianum* has a known mechanism of action, is very effective, low-cost, and most importantly, is pleasant to humans, it has the potential to be a promising cancer prevention drug (24).

Breast cancer

Research on silybinin and silymarin has shown promise. Their cytoprotective role is associated with their antioxidative and radical-scavenging capabilities. In addition, they affect specific receptor interacts with and cell signaling pathways such NF-kappa B, EGFRMAPK/ERK1/2, and IGF-receptor signaling. Silymarin also inhibits the growth of breast cancer by lowering the release of vascular endothelial growth factor (VEGF) and matrix metalloproteinase-2 (MMP-2)(25).

Skin cancer

The anti-cancer effects of silymarin on skin cancer have been studied. It has an antiangiogenic impact and may inhibit mitogenic signaling pathways. Silymarin and silybinin have proven the ability to inhibit angiogenesis, induce apoptosis, modify cell signaling pathways, and inhibit the growth of cancer cells in a variety of cancer models. It has also been shown that silymarin reduces the synthesis of MDA-DNA adducts and serum markers associated with hepatocellular carcinoma. A key element of silymarin's potential as a cancer treatment is its ability to reduce multidrug resistance, which frequently provides a barrier to effective cancer therapy. Silymarin decreases drug transporters such P-glycoprotein (P-gp), MRP1, and BRCP, increasing the absorption and bioavailability of chemotherapy medicines in cancer cells (26).

Lung cancer

The potential anti-cancer effects of silymarin on lung cancer have been explored in studies. The methods suppress growth factors and down-regulate EGFR signaling, which gives tumor cells anti-cancer efficacy.

Prostate cancer

Studies have examined how silymarin and silybinin affect prostate cancer in prostate cancer cells, they block growth factors, alter cell cycle regulators, and induce apoptosis. Silymarin also decreases the synthesis of catenin, which can prevent the growth of hepatocellular carcinoma cells**.**

Antioxidant properties

The capacity of milk thistle to reacted with essential biological ROS or oxidants, such as superoxide an ion radical (O_2), hydrogen peroxide (H_2O_2), hydroxyl radical (OH), and hypochlorus acid (HOCl), was used to a ssess the plant's antioxidant qualities (27).

Anti-inflammatory activity

The anti-inflammatory properties of silymarin originate from its suppression of nuclear factor-κB (NF-κB), a transcription factor that controls and arranges the expression of several genes linked to inflammation, cell survival, differentiation, and growth.

Mushroom poisoning

The most important application of silymarin is the management of poisoning caused by Amanita mushrooms. Amanitin and phalloidin, two highly effective hepatotoxins, are found in amanita mushrooms. If silymarin was given within 24 h, severe liver damage (as well as mortality) may be prevented (28).

Hypocholesterolaemia activity

A research study into the effects of silymarin and its polyphenolic fraction on rats given a high-cholesterol diet showed that silymarin lowered the levels of cholesterol in the rats' liver and plasma (29). Silymarin has been shown to inhibit HMG-CoA reductase activity in vitro, improve LDL binding to rat hepatocytes, reduce

liver cholesterol in high-cholesterol diet rats, and lower plasma and LDL-cholesterol levels in hyperlipidaemic rats. The impact of silymarin and its polyphenolic fraction (PF) on cholesterol absorption in rats on a high cholesterol diet (HCD) was investigated**.** In rats given HCD, silymarin and PF dramatically decreased the absorption of cholesterol and caused significant decreases in the liver's cholesterol and triacylglycerol (TAG) levels. These results indicate that silymarin and its polyphenolic component may be responsible for the beneficial alterations in the liver's lipid content and plasma cholesterol lipoprotein profile by inhibiting the absorption of cholesterol (30).

Antituberculosis activity

Patients with tuberculosis were given one Silymarin (140 mg) tablet every 8 hours after using antituberculosis medications. Silymarin had no significant negative effects after two and four weeks. In several studies, this dose of Silymarin was administered for 8 weeks with no harmful side effects. Furthermore, consuming 140 mg of Silymarin orally twice a day for 2 months was safe with no observed negative effects. In clinical research involving tuberculosis patients, oral administration of 140 mg of Silymarin three times a day for 15 days was found to be safe and effective. However, there were some digestive difficulties like nausea, vomiting, and anorexia identified (31).

Immune deficiency virus (HIV)

HIV-positive patients were administered 150 mg/d of silymarin for 15 days in order to examine its impact on the pharmacokinetics of darunavir-ritonavir. In this investigation, 15 experimental males were given the darunavir-ritonavir medication along with silymarin. Silymarin was safer and more bioavailable when taken with ritonavir and darunavir (32). Some other activities shown in Figure 3.

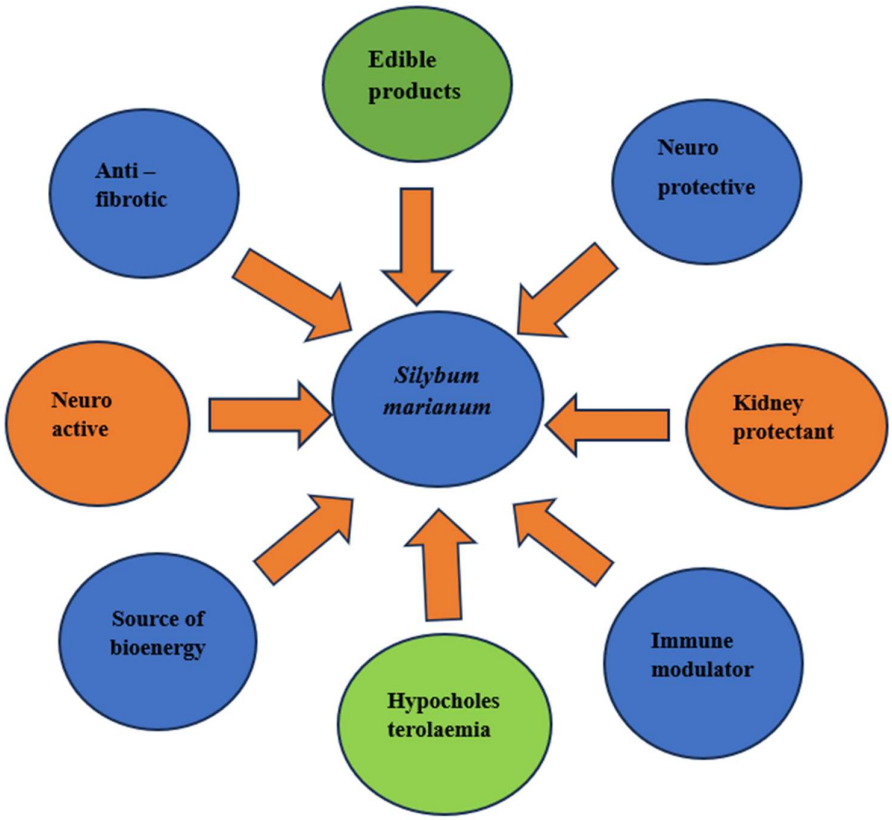

Fig 3: Ethnopharmacology of *Silybum marianum*

CONCLUSION

From this review we can conclude that the plant *Silybum marianum* is a useful medicinal plant which is mostly found in mediterranean region. It contains silymarin as a chief constituent. Different parts of the plant containing silymarin shows various pharmacological activities. This review also explains the plant's morphology, chemical constituents, habitat and distribution. It highlights the potential of *S. marianum* in preventing liver

diseases, cancer and other health conditions. With the help of this article, we came to know a complete ethnopharmacology of *Silybum marianum*. It represents a promising Phyto therapeutic agent with a rich history of traditional use. By further studies *Silybum marianum* may become a valuable addition to the modern medicine.

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