

# Nutritional and Therapeutic Potential of Milk Thistle: A Review of Its Role in Liver Health and Beyond

Ayesha Shoukat\*

Department of Human Nutrition and Dietetics, Minhaj University, Lahore 54700, Pakistan

\*2020F-mulbscn-015@mul.edu.pk

## ABSTRACT

The Mediterranean-native flowering herb milk thistle (*Silybum marianum*) has been utilized in traditional medicine for more than 2,000 years, mainly for its anti-inflammatory, antioxidant, and hepatoprotective qualities. In contemporary medicine, it is acknowledged for its therapeutic potential, especially for promoting liver function, and is called "oont katara" in Urdu. Plant seeds contain an active component called silymarin, which protects liver cells from inflammation, oxidative stress, and toxins. Research has demonstrated its efficacy in treating liver problems such as cirrhosis, hepatitis, and fatty liver disease. Because of its anti-inflammatory and antioxidant properties, milk thistle may help treat diabetes, heart disease, and some types of cancer in addition to liver function. This review will explore the nutritional and therapeutic potential of milk thistle, its bioactive constituents, its mechanism of action, therapeutic uses, safety profile, and dosage recommendations.

Received: 24 November 2024

Accepted: 06 January 2025

Published: 26 March 2025

DOI: <https://10.51200/ijf.v2i1.5644>

**Keywords:** antioxidant; anti-inflammatory; liver health; milk thistle; silymarin

## 1. Introduction

Milk thistle (*Silybum marianum*), a member of the Asteraceae family, is a widely recognised medicinal plant native to the Mediterranean region but is now found across the globe (Adetuyi *et al.*, 2021). Known for its striking purple flowers and distinctive green leaves, which are streaked with white, the plant has been used for centuries in traditional medicine, particularly for its effects on liver health (Eita, 2022). Its name originates from the milky sap that seeps from its leaves when crushed, and it has earned the name "Oont Katara" in Pakistan due to its historical use as fodder for camels. Although various parts of the plant are used in folk remedies, the seeds are primarily harvested for their medicinal properties, especially for extracting silymarin (Abenavoli *et al.*, 2018). Silymarin, a potent flavonoid complex, is the primary bioactive component responsible for many of the therapeutic benefits attributed to milk thistle (Adetuyi *et al.*, 2021).

The medicinal potential of milk thistle extends far beyond liver health, which has been its most celebrated application (Eita, 2022). Silymarin is known for its powerful antioxidant, anti-inflammatory, and hepatoprotective properties, making it a valuable tool in the management of liver diseases such as cirrhosis, hepatitis, and fatty liver (Adetuyi *et al.*, 2021; Fallah *et al.*, 2021). Research has also shown that milk thistle may play a role in managing conditions such as diabetes, cancer, and cardiovascular diseases due to its ability to regulate blood sugar levels, reduce oxidative stress, and promote detoxification (Khazaei *et al.*, 2022; Rakasiwi *et al.*, 2024; Riaz *et al.*, 2023; Valková *et al.*, 2020). Additionally, milk thistle has been investigated for its potential to enhance skin health, support brain function, and even aid in weight management (Valková *et al.*, 2020; Bhattacharya, 2020). This review aims to explore the nutritional and

therapeutic benefits of milk thistle, with a particular focus on its impact on liver health and its expanding role in the management of various health conditions.

## 2. Active Compounds and Mechanism of Action

Silymarin, the primary bioactive component found in milk thistle, is a complex mixture of flavonolignans, including silibinin, silychristin, silydianin, and isosilybinin (Al-Saedi *et al.*, 2023; Ataei *et al.*, 2024). These compounds are responsible for the therapeutic effects of milk thistle, with silibinin being most studied for its liver-protective properties (Al-Saedi *et al.*, 2023; Ali *et al.*, 2020). Silymarin has been extensively researched for its ability to combat oxidative stress, reduce inflammation, and protect liver cells from damage, making it a powerful tool in liver health management. The antioxidant effects of silymarin are attributed to its ability to neutralise free radicals, which are unstable molecules that cause cellular damage by reacting with lipids, proteins, and DNA. This oxidative damage is a major contributor to the pathogenesis of many liver diseases, including alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD), and cirrhosis. By scavenging these free radicals, silymarin helps protect the liver from cellular injury and reduces the risk of further damage (Bhattacharya, 2020).

In addition to its antioxidant properties, silymarin also exhibits significant anti-inflammatory effects. Inflammatory cytokines, such as tumour necrosis factor-alpha (TNF- $\alpha$ ) and interleukins, play a central role in the progression of liver diseases by promoting inflammation in the liver (Abenavoli *et al.*, 2018). Silymarin has been shown to inhibit the production of these cytokines, thereby reducing inflammation and preventing further damage to the liver tissue. This mechanism is particularly beneficial in managing conditions like hepatitis and cirrhosis, where chronic inflammation leads to progressive liver damage. By modulating the inflammatory response, silymarin not only helps in treating existing liver conditions but also plays a role in preventing the onset of liver diseases in individuals at risk.

Another key aspect of silymarin's therapeutic potential is its ability to promote liver cell regeneration. The liver is a highly regenerative organ, capable of repairing itself after injury; however, in cases of chronic liver damage, this regenerative capacity can be impaired (Rakasiwi *et al.*, 2024). Silymarin has been shown to stimulate protein synthesis and enhance the regenerative process by promoting the production of key molecules involved in liver cell repair. One of the most notable molecules in this process is glutathione, a powerful antioxidant that plays a crucial role in the detoxification process in the liver. Silymarin has been found to increase the levels of glutathione in hepatocytes, thus improving the liver's ability to neutralise harmful substances such as toxins, alcohol, and viral pathogens. Glutathione also helps in maintaining the integrity of liver cell membranes, which are vital for cellular function and communication (Adetuyi *et al.*, 2021).

Furthermore, silymarin helps stabilise liver cell membranes, preventing the leakage of enzymes and other cellular contents that could be harmful to surrounding tissue (Mammel *et al.*, 2021). This membrane-stabilising property is significant in protecting the liver from damage caused by alcohol, drugs, and viral infections, which can disrupt the structural integrity of liver cells. By maintaining membrane stability, silymarin contributes to the preservation of liver function and minimises the extent of liver damage in cases of acute or chronic injury. Silymarin's hepatoprotective effects are not limited to its antioxidant, anti-inflammatory, and regenerative properties. It also helps in modulating various signalling pathways that are involved in liver function and cellular response to stress (Ben Hsouna *et al.*, 2022). For instance, silymarin has been shown to activate nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that regulates the expression of antioxidant and detoxification enzymes (Anandhan *et al.*, 2023). This activation enhances the liver's defence mechanisms against oxidative stress and promotes detoxification, further supporting liver health.

### 3. Health Benefits of Milk Thistle

#### 3.1 Liver Health and Hepatoprotection

Milk thistle is best known for its hepatoprotective effects. It has been used traditionally to treat liver conditions such as jaundice, hepatitis (A, B, and C), cirrhosis, and non-alcoholic fatty liver disease (Table 1). Studies have shown that silymarin can reduce liver inflammation, prevent liver cell damage, and even promote the regeneration of damaged liver cells (Denev *et al.*, 2020). By enhancing glutathione levels in the liver, silymarin helps to neutralise harmful toxins and protects the liver from oxidative damage.

Milk thistle is often used in the treatment of liver diseases related to alcohol consumption, drug toxicity, and viral infections (Elhassaneen *et al.*, 2023). Research has also suggested that milk thistle supplementation can improve liver function markers, such as Alanine aminotransferase (ALT) and aspartate aminotransferase (AST), in patients with chronic liver diseases (Elhassaneen *et al.*, 2023; Elhassaneen & Mahran, 2024).

**Table 1** Milk Thistle's Mechanisms of Action in Liver Health

Mechanism of Action	Effect on Liver Health	Source
Antioxidant Activity via Silymarin	Neutralises reactive oxygen species (ROS) and enhances expression of Nrf2 pathways	Bhattacharya, 2020
Anti-inflammatory through NF-κB Inhibition	Reduces liver inflammation by suppressing pro-inflammatory cytokines (IL-6, TNF-α)	Kamel <i>et al.</i> , 2024
Glutathione Modulation via Silybin	Increases hepatic glutathione levels and activates glutathione peroxidase enzymes	Zeb & Jamil, 2024
Hepatocyte Regeneration via IGF-1 Pathway	Promotes liver cell repair by upregulating insulin-like growth factor-1 (IGF-1)	Samee <i>et al.</i> , 2023
Cell Membrane Stabilisation via Lipid Peroxidation Inhibition	Prevents oxidative damage to hepatocyte membranes and mitigates necrosis	Malkani <i>et al.</i> , 2020

#### 3.2 Cardiovascular Health

Milk thistle has demonstrated significant potential in improving cardiovascular health, primarily through its anti-inflammatory and antioxidant effects. Chronic inflammation is a key player in the development of cardiovascular disease (CVD), as it accelerates the process of atherosclerosis, where fatty plaques accumulate in the arteries, leading to restricted blood flow. By reducing inflammation, milk thistle helps to mitigate the risk factors associated with heart disease, including high blood pressure, poor blood circulation, and the development of arterial plaque. The active compounds in milk thistle, particularly silymarin, have been shown to inhibit the activity of inflammatory cytokines, which are proteins that play a pivotal role in driving the inflammatory process. This action not only helps reduce overall inflammation but also reduces the risk of atherosclerosis and other cardiovascular complications (Emadi *et al.*, 2022).

In addition to its anti-inflammatory effects, milk thistle also acts as a powerful antioxidant. Oxidative stress, caused by an imbalance between free radicals and antioxidants in the body, is another key contributor to cardiovascular diseases (Roth *et al.*, 2020). Free radicals damage blood vessels and promote inflammation, leading to the onset of conditions such as high blood pressure, heart attack, and stroke. Milk thistle helps by neutralising free radicals, preventing the damage they cause, and protecting the endothelial cells of the blood vessels (Bencze-Nagy *et al.*, 2023). This protection ensures the smooth functioning of the blood vessels and may help prevent conditions like endothelial dysfunction, a precursor to CVD.

Moreover, milk thistle has been found to modulate blood sugar levels, which is especially beneficial for individuals with diabetes, a significant risk factor for cardiovascular disease. Diabetes leads to higher glucose levels in the blood, which can damage the blood vessels and increase the risk of heart disease. Studies have shown that silymarin, the key component of milk thistle, may improve insulin sensitivity and

enhance glucose metabolism (Fuchs *et al.*, 2021). By stabilising blood sugar levels, milk thistle helps prevent diabetic complications, including cardiovascular damage. Furthermore, milk thistle's potential to improve lipid profiles by reducing levels of Low-Density Lipoprotein (LDL) cholesterol and triglycerides while increasing High-Density Lipoprotein (HDL) cholesterol further supports its cardiovascular protective effects. This makes milk thistle a valuable addition to the diet of individuals with diabetes or those at risk of developing heart disease.

### 3.3 Anti-Inflammatory and Antioxidant Effects

Milk thistle's anti-inflammatory properties are well-documented and contribute significantly to its therapeutic effects in various chronic diseases, including cardiovascular disease, liver disorders, and neurodegenerative conditions. Inflammatory cytokines and enzymes such as cyclooxygenase-2 (COX-2) and tumour necrosis factor-alpha (TNF- $\alpha$ ) are key mediators of inflammation. They are implicated in the pathogenesis of conditions like arthritis, diabetes, and cardiovascular disease. Milk thistle helps reduce the levels of these inflammatory markers, thus reducing systemic inflammation and potentially alleviating symptoms of chronic diseases (Ali *et al.*, 2020).

The antioxidant activity of milk thistle is another reason for its wide-ranging health benefits. Silymarin, the primary active compound in milk thistle, scavenges free radicals and reduces oxidative stress. Free radicals are highly reactive molecules that can damage cells, proteins, and DNA, contributing to ageing and the development of diseases like Alzheimer's disease, Parkinson's disease, cancer, and cardiovascular disease. By neutralising these harmful molecules, milk thistle protects the body from oxidative damage, helping to preserve the integrity of cells and tissues (Denev *et al.*, 2020). This antioxidant effect is particularly beneficial for the brain, as it can protect neurons from oxidative damage, improve cognitive function, and reduce the risk of neurodegenerative diseases. In addition, the reduction in oxidative stress provided by milk thistle can enhance the body's natural defense mechanisms, making it a valuable tool in preventing the onset of chronic diseases associated with ageing and environmental toxins. Milk thistle's ability to improve antioxidant defenses is also closely linked to its role in liver health, as the liver is a primary site of detoxification. Through its detoxifying effects, milk thistle helps prevent the buildup of harmful substances in the body, further promoting overall health and longevity (Elhassaneen *et al.*, 2023; Elhassaneen & Mahran, 2024; Emadi *et al.*, 2022).

### 3.4 Detoxification and Kidney Health

The detoxifying properties of milk thistle are particularly beneficial for individuals exposed to environmental toxins, alcohol, drugs, or other harmful substances. The liver plays a crucial role in detoxifying the body by filtering out toxins and waste products from the blood. Milk thistle enhances liver detoxification by promoting the production of glutathione, a potent antioxidant and detoxifier. By supporting liver function, milk thistle aids the liver in eliminating harmful substances, such as heavy metals, pollutants, and metabolic waste, from the bloodstream (Erdoğan *et al.*, 2024; Fanoudi *et al.*, 2020; Grant *et al.*, 2024).

In addition to its liver-supporting detoxification role, milk thistle also has a beneficial impact on kidney health. The kidneys are responsible for filtering waste products from the blood, and their function is closely linked to the liver's ability to detoxify the body. By improving liver detoxification, milk thistle indirectly supports kidney function, enhancing the body's ability to remove waste products and toxins. This is particularly important for individuals who are exposed to environmental pollutants or who have conditions such as chronic kidney disease (CKD), where toxin buildup can worsen the condition. Milk thistle's antioxidant and anti-inflammatory effects also help protect kidney cells from oxidative damage and inflammation, which can contribute to kidney dysfunction. Milk thistle has shown promise in improving kidney health by protecting the kidneys from toxins, reducing inflammation, and supporting the kidneys' ability to remove harmful substances. This makes milk thistle a valuable supplement for individuals with liver or kidney conditions or those exposed to harmful toxins, as it enhances both detoxification and overall kidney health (Fanoudi *et al.*, 2020).

### 3.5 Hormonal Modulation and Thyroid Health

Milk thistle has been shown to play a significant role in hormonal modulation, particularly in balancing estrogen levels. The liver is essential for metabolising and clearing excess estrogen from the body. In conditions where there is estrogen dominance, such as polycystic ovary syndrome (PCOS), endometriosis, and hormone-sensitive breast cancer, the liver's ability to detoxify and eliminate excess estrogen is crucial for managing symptoms (Patel *et al.*, 2023; Negm & Aboraya, 2023). By supporting liver function and enhancing its detoxification processes, milk thistle helps reduce the accumulation of estrogen, thereby alleviating symptoms associated with estrogen dominance (Riaz *et al.*, 2024; Tedesco & Guerrini, 2023).

In addition to its effects on estrogen, milk thistle also has potential benefits for thyroid health. Thyroid hormones are critical for regulating metabolism, energy production, and overall hormonal balance. Milk thistle supports thyroid function by enhancing the conversion of Thyroxine (T4) into Triiodothyronine (T3) within the liver. The triiodothyronine (T3) is the form of thyroid hormone that exerts the majority of its effects on metabolism. By improving this conversion, milk thistle can help optimise thyroid function, which is essential for maintaining proper metabolic rates and supporting overall energy levels. This makes milk thistle particularly useful for individuals with hypothyroidism or those at risk of thyroid dysfunction. Additionally, milk thistle's antioxidant and anti-inflammatory properties may help reduce inflammation in the thyroid gland, which is beneficial for individuals with autoimmune thyroid disorders like Hashimoto's thyroiditis. By reducing inflammation, milk thistle may help prevent further damage to thyroid cells, supporting better thyroid function over time (Samee *et al.*, 2023; Malkani *et al.*, 2020; Mirhashemi *et al.*, 2022).

### 3.6 Memory and Brain Health

While milk thistle is primarily known for its liver-protective benefits, its antioxidant and anti-inflammatory properties also have a positive impact on brain health. Oxidative stress and inflammation are key contributors to the development of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and other forms of cognitive decline (He & Fan, 2024). By reducing oxidative damage in brain cells, milk thistle helps protect against the cellular ageing process that is often linked to these conditions. Silymarin, the active compound in milk thistle, acts as a powerful antioxidant that scavenges free radicals in the brain, helping to preserve the integrity of neurons and improve cognitive function (Khalil *et al.*, 2022; Kamel *et al.*, 2024).

Furthermore, chronic inflammation in the brain can lead to neuroinflammation, which plays a significant role in the progression of neurodegenerative diseases. Milk thistle helps inhibit the release of pro-inflammatory cytokines and enzymes, reducing neuroinflammation and thus lowering the risk of conditions like dementia and Alzheimer's disease. Milk thistle's ability to enhance blood flow to the brain may also contribute to better cognitive function by ensuring an adequate supply of oxygen and nutrients to brain cells. Some studies have suggested that milk thistle may enhance memory, learning ability, and overall cognitive function (Samee *et al.*, 2023). These effects may be particularly beneficial for aging individuals who are experiencing cognitive decline or for those looking to protect their brain health over time. By supporting both antioxidant and anti-inflammatory pathways, milk thistle may offer a natural and effective strategy to maintain brain health and cognitive function throughout life (He & Fan, 2024).

### 3.7 Skin Health and Anti-Aging

Milk thistle is gaining recognition for its potential in promoting skin health and its anti-ageing effects. The skin, like other organs, is vulnerable to oxidative stress caused by environmental factors such as UV radiation, pollution, and smoking. These stressors contribute to skin ageing, including the formation of wrinkles, fine lines, and age spots (He & Fan, 2024). The antioxidant properties of silymarin, the active ingredient in milk thistle, help protect skin cells from oxidative damage, which may reduce the visible signs of ageing and maintain skin health (Ataei *et al.*, 2024).

Milk thistle also plays a role in protecting the skin from UV-induced damage. UV radiation is one of the leading causes of premature skin aging and skin cancer (Erdoğan *et al.*, 2024). Studies have shown that silymarin can absorb UV radiation, thereby preventing skin cells from oxidative damage caused by sun exposure (Javeed *et al.*, 2022). This protective effect can help reduce the risk of developing sunburns, age spots, and other forms of UV-related skin damage. In addition to its antioxidant properties, milk thistle's anti-inflammatory effects may help manage skin conditions such as acne, eczema, and psoriasis. Inflammation is a major factor in many chronic skin disorders, and by reducing systemic inflammation, milk thistle may alleviate symptoms associated with these conditions. Its ability to improve liver function also contributes to its skin benefits, as a healthy liver plays a crucial role in detoxifying the body and eliminating toxins that can affect the skin (Negm & Aboraya, 2023; Khalil *et al.*, 2022; Kamel *et al.*, 2024).

Milk thistle's ability to improve skin texture and reduce visible signs of ageing is also attributed to its ability to promote collagen production. Collagen is a protein that provides structure and elasticity to the skin. By enhancing collagen synthesis, milk thistle may help maintain skin's firmness and elasticity, reducing sagging and wrinkles. This makes milk thistle not only beneficial for overall skin health but also for individuals looking to improve the appearance and longevity of their skin. Together, these properties position milk thistle as a promising natural remedy for skin health, anti-aging, and the prevention of chronic skin conditions. By protecting the skin from oxidative stress, reducing inflammation, and supporting detoxification, milk thistle helps maintain youthful, healthy skin (Negm & Aboraya, 2023; Rakasiwi *et al.*, 2024).

### 3.8 Potential Role in Cancer Prevention

Emerging research indicates that milk thistle may have promising anti-cancer properties, primarily due to its antioxidant and anti-inflammatory effects (Ali *et al.*, 2020). Cancer development is often driven by oxidative stress and chronic inflammation, both of which are mitigated by the active compounds found in milk thistle, particularly silymarin. By neutralising free radicals and reducing inflammatory markers, milk thistle may help reduce the likelihood of cancer initiation and progression. One of the key areas where milk thistle has shown potential is in liver cancer. The liver is a common site for cancer development due to its role in detoxifying harmful substances. Studies have indicated that milk thistle may inhibit the growth of liver cancer cells and prevent the spread of metastases. It may also enhance the effectiveness of chemotherapy by protecting healthy liver cells from the toxic effects of cancer treatments (Mirhashemi *et al.*, 2022).

Milk thistle's potential extends beyond liver cancer. Research suggests that silymarin may also play a role in inhibiting the growth of breast and prostate cancer cells (Ali *et al.*, 2020; Ataei *et al.*, 2024). In breast cancer, milk thistle's ability to modulate estrogen metabolism is particularly relevant. Estrogen is a known driver of many breast cancer types, and by helping the liver clear excess estrogen from the body, milk thistle could serve as a supportive therapy for hormone-sensitive breast cancers. Similarly, prostate cancer, which can be influenced by both estrogen and testosterone imbalances, may benefit from milk thistle's estrogen-modulating properties (Riaz *et al.*, 2024; Tedesco & Guerrini, 2023). Additionally, milk thistle has been studied for its potential to enhance the immune response against tumors. Some studies suggest that silymarin can activate immune cells such as T-cells and natural killer (NK) cells, which are crucial for identifying and destroying cancer cells (Ali *et al.*, 2020; Valková *et al.*, 2020; Zeb & Jamil, 2024). While more clinical trials are needed, milk thistle presents a promising natural option in cancer prevention and therapy, particularly as part of a broader integrative approach.

### 3.9 Varicose Veins

Milk thistle has also been found to offer benefits in alleviating varicose veins, a condition commonly associated with poor circulation and hormonal imbalances. One of the contributing factors to varicose veins, particularly in women, is elevated estrogen levels. High estrogen can weaken the walls of blood vessels, making them more prone to bulging and twisting, which leads to the formation of varicose veins. By promoting liver detoxification, milk thistle helps regulate and clear excess estrogen from the body, thus

potentially reducing the risk of developing or worsening varicose veins (Valková *et al.*, 2020).

Furthermore, milk thistle's anti-inflammatory effects can help reduce the inflammation in blood vessels that is often seen in varicose veins. Chronic inflammation can damage blood vessel walls and exacerbate the condition. Through its antioxidant properties, milk thistle may also protect the blood vessel endothelium (the inner lining of blood vessels) from oxidative damage, which can worsen vein health. This combination of hormonal balance, inflammation reduction, and antioxidant protection makes milk thistle a valuable natural remedy for individuals dealing with varicose veins (Negm & Aboraya, 2023; Rakasiwi *et al.*, 2024). In addition to liver detoxification, when combined with a liver-friendly diet such as the ketogenic diet (which supports liver health and reduces inflammation), milk thistle may help prevent further vein damage and improve overall circulation. Regular consumption of milk thistle may also enhance vascular health, promoting better blood flow and reducing the appearance of varicose veins over time (Javeed *et al.*, 2022). As a complementary therapy, milk thistle may help prevent the worsening of varicose veins and support the health of the circulatory system.

### 3.10 Prostate Health and Enlargement

Prostate enlargement, also known as benign prostatic hyperplasia (BPH), is a common condition in older men, often characterised by symptoms such as frequent urination, difficulty urinating, and erectile dysfunction (Emadi *et al.*, 2022; Erdoğan *et al.*, 2024). Hormonal imbalances, particularly high levels of estrogen relative to testosterone, play a role in the development and progression of BPH. Estrogen can stimulate the growth of prostate tissue, contributing to its enlargement. Milk thistle's ability to support liver function and regulate estrogen levels may therefore be particularly beneficial in managing prostate health (Mirhashemi *et al.*, 2022). By aiding the liver in detoxifying and clearing excess estrogen, milk thistle helps restore hormonal balance. This can reduce the growth-promoting effects of estrogen on the prostate, potentially reducing the size of the prostate and alleviating symptoms of BPH. Furthermore, milk thistle's anti-inflammatory properties may help reduce the inflammation commonly seen in the prostate in individuals with BPH. Chronic inflammation is a contributing factor in the enlargement and discomfort associated with the condition, and by mitigating this inflammation, milk thistle may provide symptom relief.

Milk thistle may also support urinary function by improving overall kidney and liver health. The liver's role in detoxification and the kidneys' function in waste removal are crucial for maintaining healthy urinary output (Negm & Aboraya, 2023; Rakasiwi *et al.*, 2024). With better overall detoxification, the body may be able to more effectively manage waste products, which in turn may reduce the strain on the prostate and support healthy urinary function. In addition to liver detoxification and inflammation reduction, milk thistle's antioxidant effects may protect prostate cells from oxidative damage, which can contribute to the ageing of prostate tissue. This may help prevent further damage to the prostate and improve overall prostate health. For men experiencing symptoms of BPH or those seeking to maintain prostate health as they age, milk thistle offers a natural and supportive therapy (Khalil *et al.*, 2022; Kamel *et al.*, 2024; Malkani *et al.*, 2020; Mirhashemi *et al.*, 2022).

## 4. Dosage and Administration

Milk thistle is widely available in various forms, including capsules, tablets, liquid extracts, and powdered forms. The standard dosage of milk thistle typically ranges from 200 to 400 mg per day, divided into two to three doses. For liver protection, higher doses (up to 2100 mg/day) may be used in acute liver conditions, under medical supervision (Table 2). The bioavailability of silymarin is relatively low, around 20-50%, which is why standardised extracts are recommended for optimal effects (Tedesco & Guerrini, 2023; Gillessen & Schmidt, 2020).

**Table 2** Dosage, Administration, and Safety Profile of Milk Thistle

Formulation/Study	Dosage	Duration	Population/Condition	Reported Adverse Events	Source	NCT Number
Clinical Trials (General)	Up to 420 mg/day (recommended dose)	Up to 4 years	Liver disease, general use	Minor adverse events (< 4%), no serious adverse events or deaths	Natural Medicines Comprehensive Database, 2018; Gillessen & Schmidt, 2020	N/A
Clinical Trials (High Dose)	2100 mg/day	Up to 48 weeks	Liver disease	Minor adverse events, gastrointestinal discomfort (diarrhea, dyspepsia)	Natural Medicines Comprehensive Database, 2018; Gillessen & Schmidt, 2020	NCT00680342
Randomised Phase I Dose Ascending Trial	140 mg (recommended dose), 280 mg, 560 mg, 700 mg every 8 hours	7 days	Chronic hepatitis C (non-cirrhotic)	Mild-to-moderate nausea and headache (resolved within 24 hours)	Hawke <i>et al.</i> , 2010; Gillessen & Schmidt, 2020	NCT00938899
Randomised Trial in Chronic Hepatitis C (Egyptian Study)	125 mg, three times a day	12 months	Chronic hepatitis C	Abdominal colic/discomfort, fatigue, headache, diarrhea	Tanamly <i>et al.</i> , 2004; Gillessen & Schmidt, 2020	NCT02487030
Case Report (Serious Adverse Event)	Standardised preparation	N/A	General use	Serious adverse event (hospitalisation due to nausea, colicky pain, diarrhea, vomiting)	Saller <i>et al.</i> , 2008; Gillessen & Schmidt, 2020	N/A
Common Side Effects (Open-Label Trials)	Varies	N/A	General use	Gastrointestinal discomfort (diarrhea, nausea, dyspepsia)	Saller <i>et al.</i> , 2008; Gillessen & Schmidt, 2020	N/A
Animal Studies (Feed Additive/Ingredient)	Varies (silymarin extract, seed/cake)	Varies (from acute to chronic treatment)	Farm animals (dogs, cats, equine athletes, aquaculture)	No serious adverse events reported	Tedesco & Guerrini, 2023	N/A

N/A – Not Applicable

NCT – National Clinical Trials

## 5. Side Effects and Precautions

Milk thistle is generally considered safe for most people when taken in recommended doses. However, some individuals may experience mild side effects, including gastrointestinal discomfort, headaches, or skin reactions such as pruritus (itching). It is important to note that milk thistle can interact with certain medications, particularly those processed by the liver, including statins, anticoagulants, and oral contraceptives (Abenavoli *et al.*, 2018; Samee *et al.*, 2023). Therefore, individuals taking medications should consult a healthcare provider before starting milk thistle supplementation.

## 6. Conclusion and Future Direction

Overall, while milk thistle, particularly its active compound silymarin, has demonstrated significant therapeutic potential in liver health and various other conditions such as cardiovascular disease, hormone regulation, cognitive function, and skin health, more comprehensive research is needed to fully understand its mechanisms of action and efficacy. Although the existing evidence highlights its antioxidant, anti-inflammatory, and detoxifying effects, further large-scale clinical trials are necessary to determine optimal dosages and long-term safety for different health conditions. Future studies should also explore the synergistic effects of milk thistle with other natural remedies or conventional therapies and investigate its role in chronic diseases beyond liver-related issues. Continued research will help unlock its full potential, positioning milk thistle as a valuable addition to integrative health practices.

## References

Abenavoli, L., Izzo, A. A., Milić, N., Cicala, C., Santini, A., & Capasso, R. (2018). Milk thistle (*Silybum marianum*): A concise overview on its chemistry, pharmacological, and nutraceutical uses in liver diseases. *Phytotherapy Research*, 32(11), 2202–2213.

Adetuyi, B. O., Omolabi, F. K., Olajide, P. A., & Oloke, J. K. (2021). Pharmacological, biochemical and therapeutic potential of milk thistle (silymarin): A review. *World News of Natural Sciences*, 37, 75–91.

Al-Saedi, J. H. M., Mernea, M., Anghelescu, G. D. C., NIȚU, C. D., Stoian, G., & Mihailescu, D. (2023). The inhibitory effect of *Silybum marianum* (milk thistle) seeds extract on serum albumin glycation by glucose, fructose, and galactose. *Romanian Journal of Biophysics*, 33(2).

Ali, B. S., ElSayed, A. I., Doheem, M. A., Eita, A. M. A., & Omar, A. A. (2020). Effect of milk thistle (*Silybum marianum (L.) Gaertn*) seed extract on bacterial activities and growth of human liver cancer cells. *J. Biotechnol. Res*, 6, 27–33.

Anandhan, A., Dodson, M., Shakya, A., Chen, J., Liu, P., Wei, Y., Tan, H., Wang, Q., Jiang, Z., Yang, K., Garcia, J., Chambers, S.K., Chapman, E., Ooi, A., Yang-Hartwich, Y., Stockwell, B.R., & Zhang, D. (2023). NRF2 controls iron homeostasis and ferroptosis through HERC2 and VAMP8. *Science Advances*, 9.

Ataei, S., Mahdian, M. R., Ghaleiha, A., Matinnia, N., & Nili-Ahmabadi, A. (2024). Silymarin improves thyroid function in lithium-treated bipolar patients: A randomized, double-blind, placebo-controlled pilot study. *Current Drug Therapy*, 19(3), 346–353.

Ben Hsouna A, Hfaiedh M, Ben Slima S, Romdhane WB, Akacha BB, Bouterfa MT, Dhifi W, Mnif W, Brini F, Ben Saad R, Ben Salah R. (2022). Antioxidant and hepatoprotective effects of novel heteropolysaccharide isolated from *Lobularia maritima* on CCl<sub>4</sub>-induced liver injury in rats. *Food Science & Nutrition*, 10, 2271-2284.

Bencze-Nagy, J., Strifler, P., Horváth, B., Such, N., Farkas, V., Dublez, K., & Pál, L. (2023). Effects of Dietary Milk Thistle (*Silybum marianum*) Supplementation in Ducks Fed Mycotoxin-Contaminated Diets. *Veterinary Sciences*, 10.

Bhattacharya, S. (2020). Milk thistle seeds in health. In *Nuts and Seeds in Health and Disease Prevention* (pp. 429–438). Academic Press.

Denev, P., Ognyanov, M., Georgiev, Y., Teneva, D., Klisurova, D., & Yanakieva, I. Z. (2020). Chemical composition and antioxidant activity of partially defatted milk thistle (*Silybum marianum L.*) seeds. *Bulg. Chem. Commun*, 52, 182–187.

Eita, A. A. B. (2022). Milk thistle (*Silybum marianum (L.) Gaertn.*): An overview about its pharmacology and medicinal uses with an emphasis on oral diseases. *Journal of Oral Biosciences*, 64(1), 71–76.

Elhassaneen, Y. A., Nasef, A. Z., Arafa, R. S., & Bayomi, A. I. (2023). Bioactive compounds and antioxidant activities of milk thistle (*Silybum marianum*) extract and their potential roles in the prevention of diet-induced obesity complications. *American Journal of Food Science and Technology*, 11(3), 70–85.

Elhassaneen, Y. A. E. A., & Mahran, M. Z. (2024). Potential protective effects of milk thistle (*Silybum Marianum L.*) seeds against Benzo[a]pyrene-induced hepatic and nephritic injuries in rats: Biochemical and histopathological studies. *Alexandria Science*

Exchange Journal, 45(1), 131–152.

Emadi, S. A., Rahbardar, M. G., Mehri, S., & Hosseinzadeh, H. (2022). A review of therapeutic potentials of milk thistle (*Silybum marianum L.*) and its main constituent, silymarin, on cancer, and their related patents. *Iranian Journal of Basic Medical Sciences*, 25(10), 1166.

Erdoğan, Ü., Gökçe, E. H., Muhammed, M. T., Önem, E., Erten, A. A., & Süleymanoğlu, B. (2024). Milk thistle extracts could enhance the UV-protection efficiency and stability of mineral filters in sunscreen formulations. *Journal of Photochemistry and Photobiology A: Chemistry*, 450, 115460.

Fanoudi, S., Alavi, M. S., Karimi, G., & Hosseinzadeh, H. (2020). Milk thistle (*Silybum Marianum*) as an antidote or a protective agent against natural or chemical toxicities: A review. *Drug and Chemical Toxicology*, 43(3), 240–254.

Fallah M, Davoodvandi A, Nikmanzar S, Aghili S, Mirazimi SM, Aschner M, Rashidian A, Hamblin MR, Chamanara M, Naghsh N, Mirzaei H. (2021). Silymarin (milk thistle extract) as a therapeutic agent in gastrointestinal cancer. *Biomedicine & Pharmacotherapy*, 142, 112024.

Fuchs A, Samovski D, Smith GI, Cifarelli V, Farabi SS, Yoshino J, Pietka T, Chang SW, Ghosh S, Myckatyn TM, Klein S. (2021). Associations among adipose tissue immunology, inflammation, exosomes and insulin sensitivity in people with obesity and non-alcoholic fatty liver disease. *Gastroenterology*, 161(3), 968-981.

Gillessen, A., & Schmidt, H. H. J. (2020). Silymarin as supportive treatment in liver diseases: A narrative review. *Advances in Therapy*, 37(4), 1279-1301.

Grant, J. E., Driessens, C., & Chamberlain, S. R. (2024). Silymarin (Milk Thistle) treatment of adults with gambling disorder: A double-blind, placebo-controlled trial. *Clinical Neuropharmacology*, 47(2), 54-58.

Hawke RL, Schrieber SJ, Soule TA, Wen Z, Smith PC, Reddy KR, Wahed AS, Belle SH, Afdhal NH, Navarro VJ, Berman J. (2010). Silymarin ascending multiple oral dosing phase I study in noncirrhotic patients with chronic hepatitis C. *The Journal of Clinical Pharmacology*, 50(4), 434-449.

He, M., & Fan, L. (2024). Evaluation of anti-aging effect of percutaneous application of *Silybum marianum* extract. *China Surfactant Detergent & Cosmetics* (2097-2806), 54(8).

Javeed A, Ahmed M, Sajid AR, Sikandar A, Aslam M, Hassan TU, Dogar S, Nazir Z, Ji M, Li C. (2022). Comparative assessment of phytoconstituents, antioxidant activity and chemical analysis of different parts of milk thistle *Silybum marianum L.* *Molecules*, 27(9), 2641.

Kamel, N. M., El-Sayed, S. S., El-Said, Y. A., El-Kersh, D. M., Hashem, M. M., & Mohamed, S. S. (2024). Unlocking milk thistle's anti-psoriatic potential in mice: Targeting PI3K/AKT/mTOR and KEAP1/NRF2/NF-κB pathways to modulate inflammation and oxidative stress. *International Immunopharmacology*, 139, 112781.

Khalil, A. A., Abd-Elhakim, Y. M., Said, E. N., Moselhy, A. A., Abu-Elsaoud, A. M., & El-Houseiny, W. (2022). Milk thistle and co-enzyme Q10 fortified diets lessen the nickel chloride-induced neurotoxic and neurobehavioral impairments in *Oreochromis niloticus* via regulating the oxidative stress response, acetylcholinesterase activity, and brain nickel content. *Aquaculture*, 553, 738102.

Khazaei, R., Seidavi, A., & Bouyeh, M. (2022). A review on the mechanisms of the effect of silymarin in milk thistle (*Silybum marianum*) on some laboratory animals. *Veterinary Medicine and Science*, 8(1), 289-301.

Malkani, N., Naeem, A., Ijaz, F., Mumtaz, S., Ashraf, S., & Sohail, M. I. (2020). *Silybum marianum* (milk thistle) improves vancomycin-induced nephrotoxicity by downregulating apoptosis. *Molecular Biology Reports*, 47, 5451-5459.

Mammel, A. E., Huang, H., Gunn, A. L., Choo, E., & Hatch, E. M. (2021). Chromosome length and gene density contribute to micronuclear membrane stability. *Life Science Alliance*, 5.

Mirhashemi, S. H., Hakakzadeh, A., Yeganeh, F. E., Oshidari, B., & Rezaee, S. P. (2022). Effect of 8 weeks milk thistle powder (silymarin extract) supplementation on fatty liver disease in patients candidates for bariatric surgery. *Metabolism Open*, 14, 100190.

Natural Medicines Comprehensive Database. (2018). Milk thistle. <http://www.naturaldatabase.com/>.

Negm, S., & Aboraya, A. (2023). Therapeutic effects of milk thistle seeds (*Silybum marianum*) and red ginseng roots on polycystic

ovary syndrome induced by letrozole in female rats. *Journal of Qualitative Education Research*, 2023(75), 199-234.

Patel, V., Prakasam, A., & Patel, S. (2023). Chapter-3 Galactagogues Herbs for Lactating Mothers. *Natural Product Research*, 1, 41.

Rakasiwi, M. I., Taufik, M., Pamungkas, G. C., Amaanullah, M. Z., & Dewantara, I. R. (2024). Exploring the therapeutic benefits of silymarin herbal extract as a supplement to pulmonary tuberculosis treatment: A comprehensive review from laboratory to clinical trials. *Medical Scope Journal*, 6(2), 243-249.

Riaz, T., Akram, M., Laila, U., Khalil, M. T., & Mirza, M. A. (2024). Protective effect of *Silybum marianum* (Milk Thistle) on liver function in diabetic rats. *Pakistan Journal of Pharmaceutical Sciences*, 37(2), 563-570.

Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, Barengo NC, Beaton AZ, Benjamin EJ, Benziger CP, Bonny A. (2020). Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. *Journal of the American college of cardiology*, 76(25), 2982-3021.

Saller, R., Brignoli, R., Melzer, J., & Meier, R. (2008). An updated systematic review with meta-analysis for the clinical evidence of silymarin. *Forschende Komplementärmedizin/Research in Complementary Medicine*, 15(1), 9-20.

Samee A, Amir RM, Ahmad A, Watto FM, Ali M, Azam MT, Sheeraz M, Fatima H, Zahoor Z, Zahid M, Ashraf H. (2023). Effectiveness of milk thistle on human body against diseases: A comprehensive review. *Scholars Bulletin*, 9(2), 8-18.

Tanamly MD, Tadros F, Labeeb S, Makld H, Shehata M, Mikhail N, Abdel-Hamid M, Abu-Baki L, Medhat A, Magder LS, Afdhal NH. (2004). Randomized double-blinded trial evaluating silymarin for chronic hepatitis C in an Egyptian village: study description and 12-month results. *Digestive and Liver Disease*, 36(11), 752-759.

Tedesco, D. E. A., & Guerrini, A. (2023). Use of milk thistle in farm and companion animals: A review. *Planta Medica*, 89(06), 584-607.

Valková, V., Ďúranová, H., Bilčíková, J., & Habán, M. (2020). Milk thistle (*Silybum marianum*): A valuable medicinal plant with several therapeutic purposes. *The Journal of Microbiology, Biotechnology and Food Sciences*, 9(4), 836.

Zeb, A., & Jamil, M. (2024). Milk thistle protects against non-alcoholic fatty liver disease induced by dietary thermally oxidized tallow. *Heliyon*, 10(10).