Review Article

Milk thistle: A review of its phytochemistry, pharmacology and conventional uses

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Abstract

The well-known medicinal plant milk thistle (Silybummarianum) has a long history of traditional use, and a growing body of scientific study is demonstrating its therapeutic potential. In-depth information about milk thistle's phytochemistry, pharmacology, and customary usage is provided in this review article. We explore the numerous phytochemicals present in milk thistle with a focus on silymarin, which is thought to be the main bioactive component. Examining milk thistle's pharmacological attributes entails learning about its hepatoprotective, antioxidant, anti-inflammatory, and anticancer effects. We also go into the traditional and mainstream applications of milk thistle, such as detoxification, liver problems, and dietary supplements. We also highlight recent developments in the realm of complementary and alternative medicine as well as potential future uses for milk thistle. The goal of this review is to present a thorough and current understanding of milk thistle, making it a useful tool for researchers, medical experts, and those curious about the possible health advantages of this remarkable botanical.

Key words

Medicinal plant, Milk thistle, Phytochemistry, Pharmacology, Therapeutic activities.

Introduction

For millennia, people have been fascinated by and used milk thistle (Silybummarianum), a hardy flowering plant with unusual purple-petaled flowers and spiky foliage. This botanical gem has attracted a lot of interest from researchers, medical professionals, and fans due to its extensive history of traditional and modern applications. A growing corpus of scientific research has been published recently that examines the milk thistle's many facets, from its complex phytochemistry to its intriguing pharmacological capabilities and time-honored traditional usage. The potential of milk thistle as a useful natural resource for enhancing health and wellbeing is what spurs interest in it, not just by coincidence [1]. Using a variety of sources and recent studies, this review article aims to give a thorough and current analysis of milk thistle. It attempts to illuminate the plant's intricate phytochemical makeup, clarify its numerous pharmacological effects, and delve into its traditional uses in medicine.

The prominent component of milk thistle, silymarin, a combination of flavonolignans, is known for its outstanding phytochemical profile [2]. The therapeutic potential of milk thistle is based on this complex mixture of bioactive substances, which is the main area of study in both laboratory and clinical trials. Understanding milk thistle's phytochemistry is therefore essential to discovering the wide range of health benefits it offers.

The pharmacological effects of milk thistle are equally fascinating, with some of the most in-depth research being done on its hepatoprotective, antioxidant, anti-inflammatory, and anticancer actions [3]. These qualities have led to increased interest in milk thistle's potential uses in treating a range of different medical ailments in addition to making it a popular choice for individuals seeking liver support and detoxification.The traditional and conventional uses of milk thistle have been documented throughout history, spanning numerous cultures and epochs [4]. Milk thistle has been used for its alleged health-improving effects in folk treatments from Europe to Asian traditional medical systems. The historical value of the plant can be better understood by understanding these traditional usages, which can also influence present applications.

It is crucial to close the gap between conventional wisdom and modern science as the

demand for natural and complementary medicines rises. This review seeks to provide a thorough overview of the phytochemistry, pharmacology, and traditional usage of milk thistle for researchers, medical professionals, and others who are interested in the herb. We aim to contribute to the on-going investigation of milk thistle's potential in the field of integrative medicine and beyond by synthesising current knowledge and emphasising emerging research areas.

History and occurrence

Milk thistle, scientifically known as Silybummarianum L., has been used as a venerable botanical treatment for a wide range of illnesses for over two millennia. This remedy has a long folklore history and has been used in traditional medicine to treat a variety of illnesses, including liver disorders, kidney disorders, rheumatic diseases, digestive problems, cardiac irregularities, and conditions related to the gallbladder, such as jaundice, hepatitis, and cirrhosis [5]. The plant grows to astonishing heights of between 5 and 10 feet and is a statuesque biennial herb. It has distinguishing traits, including impressive spiky leaves, eye-catching, big purple flower heads, and sturdy spiny stalks. The milky-white veins that run across its leaves are one of its most unique characteristics and the source of its name [6]. The milk thistle is a native plant to many parts of the world, including Australia, South and North America, Southern Europe, North Africa, and some areas of Asia [7]. It has long been a popular salad ingredient throughout Europe, and its seeds are renowned for their galactagogue characteristics, which help lactating women [8]. This plant is mentioned as "Harshfbari" and is shown with a picture of milk thistle in the ancient literature "Al-Hashaish Dioscorides," one of the key texts in the field of traditional medicine. Its characteristics and alternate names are consistent with those in numerous sources of conventional Iranian medicine, demonstrating its continuing importance in medical customs [9]. Silybummarianum extends its protective embrace against a broad range of chemical poisons, including metals, fluoride, pesticides, and a litany of substances known to be cardiotoxic, neurotoxic, hepatotoxic, and nephrotoxic [10]. It also protects against a variety of biological toxins, including mycotoxins, snake venoms, and bacterial toxins.

Silymarin, one of its main bioactive components, has shown extraordinary potential in lowering lipid peroxidation and consequently showing strong antioxidant qualities. Additionally, it has been shown to have antidiabetic, hepatoprotective, and antihypertensive properties [11, 12]. Numerous studies have revealed the versatile medicinal properties of S. marianum. It has been demonstrated that by inducing apoptosis and producing reactive oxygen species (ROS), it reduces the viability, adhesion, and migration of malignant tumour cells. Lower glutathione levels, downregulation of important proteins like B-cell lymphoma 2 (Bcl-2) and survivin, suppression of cyclin D1 and Notch 1 intracellular domain (NICD), and an increase in Bcl-2-associated X protein (Bax) levels all contribute to these effects [13, 14].

Phytochemistry

The main and best-known component of milk thistle extract is silymarin, a complex combination that is present in the plant's leaves, seeds, and fruits [15]. Silymarin is mostly made up of flavonolignans and often makes about 70–80% of the extract. Along with other flavonoids including taxifolin, quercetin, and apigenin, silymarin contains several important flavonolignans, including silybin, isosilybin, silychristin, and silydianin [15]. Silybin stands out as the main and most physiologically active component of silymarin among these chemicals. When compared to other flavonolignans, it is frequently regarded as the foundation of milk thistle's medicinal activities and is well acknowledged for its exceptional therapeutic effects [15]. Additionally, silymarin contains

diastereomeric pairs of flavonolignans, designated A and B, with different ratios of these pairings contributing to the total composition [16]. This intricate blend of diastereomers adds to the silymarin's complexity and might affect its range of biological activities [17].

Pharmacology and conventional uses

Anti-cancer activity

Numerous researches have examined the potential of milk thistle (Silybummarianum) in the prevention and treatment of cancer, reflecting the increased interest in this herb's anti-cancer properties in recent years. There is evidence to suggest that milk thistle may have anti-cancer qualities, mostly attributed to its active component silymarin, although research is ongoing and further clinical trials are required.

Breast Cancer

Research on silymarin and silybinin has showed promise [18–19]. Their antioxidative and radical-scavenging properties are linked to their cytoprotective function. They also influence cell-signaling pathways such NF-kappa B, EGFR-MAPK/ERK1/2, and IGF-receptor signalling, as well as particular receptor interactions. By reducing the release of matrix metalloproteinase-2 (MMP-2) and vascular endothelial growth factor (VEGF), silymarin also has anti-angiogenic effects on breast cancer.

Ovarian Cancer

Although particular processes and results may differ, silymarin or silybinin has been shown to have an impact on ovarian cancer [20].

Lung cancer

Studies have looked into silymarin's possible anti-cancer properties on lung cancer. The mechanisms result in anti-cancer efficacy in tumour cells by down-regulating EGFR signalling and inhibiting growth factors [21].

Prostate Cancer

The effects of silymarin and silybinin on prostate cancer have been studied [22]. In prostate cancer cells, they cause apoptosis, modify cell cycle regulators, and inhibit growth factors. Additionally, silymarin reduces -catenin synthesis, which can stop hepatocellular carcinoma cells from proliferating.

Skin cancer

Silymarin's anti-cancer properties in skin cancer have been investigated [23]. It may suppress mitogenic signalling pathways and possess anti-angiogenic effects.

In numerous cancer models, silymarin and silybinin have shown an ability to suppress the development of cancer cells, trigger apoptosis, alter cell signalling pathways, and lessen angiogenesis. The production of MDA-DNA adducts and serum indicators linked to hepatocellular cancer has also been demonstrated to be decreased by silymarin [24]. The capacity of silymarin to decrease multidrug resistance, which frequently presents a problem in effective cancer therapy, is a crucial component of its promise as a cancer treatment. Silymarin increases the absorption and bioavailability of chemotherapeutic drugs in cancer cells by decreasing drug transporters such P-glycoprotein (P-gp), MRP1, and BRCP.

Hepatoprotective activity

Silymarin, a milk thistle component with hepatoprotective effects, has been used for many years. Silymarin is recognised to have a variety of advantageous qualities, including antioxidant, immunomodulatory, antifibrotic, antiproliferative, and antiviral effects, even if the exact mode of action is still not completely understood. It is important to keep in mind, nevertheless, that silymarin mostly excretes through bile and has a fast liver conjugation and half-life. It requires high or repeated oral doses to successfully suppress hepatic inflammation in vivo [25].

The primary sources of silymarin's hepatoprotective benefits are its capacity to scavenge free radicals and boost cellular glutathione levels. When exposed to xenobiotics, these effects result in the suppression of lipid peroxidation and increased membrane stability. In addition, silymarin has steroid-like effects by controlling nuclear expression and preventing the differentiation of stellate hepatocytes into myofibroblasts, which in turn lessens the deposition of collagen fibres. Additionally, silymarin and its main component, silybinin, promote RNA polymerase I, which improves the synthesis of ribosomal proteins [26].

Silybinin stands out for having a large impact on the levels of inflammatory cytokines like IL-2, IL-4, IFN-, and TNF- in the intra-hepatic messenger RNA (mRNA). Additionally, this substance reduces hepatocyte apoptosis while lowering alanine and aspartate aminotransferase levels [25, 26]. Silybin A and B decrease T-cell proliferation and the release of pro-inflammatory cytokines in a dose-dependent manner, according to in vitro research. In situations of chronic liver illness, silymarin taken orally in high doses has been shown to be useful in reducing hepatic inflammation [25]. Silymarin exhibits promise in preventing hepatocyte mortality brought on by high levels of circulating free fatty acids in the context of non-alcoholic fatty liver disease (NAFLD), highlighting its potential as a therapy option for this condition [27]. Silymarin and silybinin's protective properties against a variety of hepatotoxic substances, such as acute ethanol intoxication, carbon tetrachloride, cisplatin, thioacetamide, thallium, D-galactosamine, and acetaminophen, have been confirmed in animal experiments [28]. Notably, silymarin seed ethanolic extract administration dramatically lowered liver enzyme levels in rats with liver damage brought on by carbon tetrachloride. Furthermore, silymarin's ethyl acetate extracts significantly improved glutathione levels and HDL/LDL ratios in oxidative studies [26, 29].

Immunomodulatory activity

Through a flow cytometric analysis of splenocytes, the effect of silymarin on immune cell populations, in particular T-lymphocytes, has been researched. Notably, silymarin's effects on immunological performance were dose-dependent. Silymarin significantly decreased the CD3+ T-lymphocyte count and the CD4+ population at a dose of 10 mg/kg. It's interesting to note that the proliferation of phytohemagglutinin-induced T-lymphocytes increased in the group receiving the lowest dose. This suggests that silymarin may improve some elements of T-cell function at lower doses. More specifically, silymarin treatment at doses of 10 and 50 mg/kg boosted B-lymphocyte blastogenesis, especially in response to stimulation with lipopolysaccharide (LPS). However, under these circumstances, IL-2 and IL-4 expression was diminished. This shows that silymarin may modify B-lymphocyte activity and change the patterns of cytokine expression. Additionally, silymarin was found to influence inflammatory pathways. It simultaneously decreased the synthesis of IL-2 and interferon gamma (IFN-), while increasing the expression of pro-inflammatory markers such TNF-, iNOS, IL-1, and IL-6 mRNA in a dose-dependent way. This suggests that silymarin may affect inflammation in two different ways, activating certain pathways while dampening others.The nuclear translocation of transcription factor B (NF-B), a critical regulator of immunological responses, was also found to be inhibited by silymarin. As a result, it is possible that silymarin inhibits T-cell activation and proliferation via altering NF-B activity or translocation [30].

Renal protective activity

Silymarin, a bioactive ingredient produced from milk thistle, has shown promise in treating a range of renal problems and illnesses. Various models of renal damage and patients with renal impairment have been used to study its effects.

Diabetic Nephropathy

Effective reduction of renal tissue damage was achieved when silymarin was given 20 days after nine weeks of alloxan treatment in a rat model of alloxan-induced diabetes mellitus. The antioxidant properties of silymarin were demonstrated by an increase in the gene expression of important antioxidant enzymes as catalase, glutathione peroxidase, and superoxide dismutase. This shows that by reducing oxidative stress and its negative effects, silymarin may be used as a treatment for diabetic nephropathy [31].

Protection against Gentamicin-Induced Renal Damage

Both silymarin and vitamin E were observed to improve changes in blood creatinine concentrations in investigations involving dogs treated with gentamicin. This shows that silymarin, a popular antibiotic with nephrotoxic side effects, can reduce kidney damage brought on by gentamicin [32].

Renal Protection during Chemotherapy

Silymarin has shown the ability to counteract renal toxicity brought on by chemotherapy drugs like cisplatin and ifosfamide without sacrificing the effectiveness of these medicines in treating tumours. This makes silymarin a potential co-treatment to lessen the chemotherapy's renal adverse effects [33-34].

Protection against Nephrotoxicity and Renal Cancer

Ferric nitrilotriacetate (Fe-NTA), which produces reactive oxygen species and causes lipid peroxidation, is known to cause nephrotoxicity and raise the risk of kidney cancer. Silymarin has demonstrated beneficial effects against DNA-damaging compounds including 8-hydroxy guanosine and lipid peroxidation caused by Fe-NTA. The antioxidant and free radical scavenging capabilities of silymarin are responsible for these beneficial effects. The NF-B pathway, which is involved in fostering neoplastic processes, cellular inflammation, proliferation, and the prevention of apoptosis, can also be suppressed by silymarin. Silymarin is a potential treatment option for renal carcinogenesis due to its capacity to decrease NF-B activation [35].

Anti-Inflammatory Effects in Patients Receiving Peritoneal Dialysis

Silymarin was given to peritoneal dialysis patients in a human research for eight weeks at a dose of 210 mg/day to block the effects of pro-inflammatory cytokines, mainly TNF-. This is essential because TNF- may decrease bone marrow and limit erythropoiesis, which can cause haematological problems, especially in individuals with severe renal failure. A role for silymarin in treating inflammatory anaemia in peritoneal dialysis patients was suggested by the study's finding that silymarin increased haemoglobin concentrations in 40% of the patients [36].

Neuroprotective activity

Due to its high oxygen utilisation, abundance of polyunsaturated fatty acids, elevated amounts of free iron ions, and relatively limited antioxidant defences, and the brain is particularly susceptible to damage from reactive oxygen species (ROS) [37]. Silymarin, a naturally occurring substance derived from milk thistle, is being researched for its potential in treating a number of neurological diseases and has showed promise in preventing oxidative damage to the brain.

Alzheimer's disease

Protein oxidation plays a key role in the early stages of Alzheimer's disease pathogenesis. Silymarin was discovered to dramatically lessen protein oxidation in the cortex and hippocampus of aged rats when supplied at a level of 200 mg/kg/day. Given its antioxidant characteristics in the central nervous system and its capacity to cross the blood-brain barrier, this raises the possibility that silymarin may play a protective role in the fight against Alzheimer's disease [38-39].

Parkinson's disease

Silymarin, at a dose of 200 mg/kg, attenuated 6-hydroxydopamine (6-OHDA)-induced rotating behaviour in hemi-parkinsonian rats. Additionally, it shielded substantianigra pars compacta neurons from 6-OHDA damage. This suggests that silymarin has a dose-dependent neuroprotective effect against 6-OHDA-induced damage, most likely by lowering oxidative stress and working through an estrogenic route [40].

Neurotransmitter Modulation

Silymarin has also been seen to affect the levels of specific neurotransmitters in the brain. The duration of the mice's immobility was dramatically reduced by the aqueous extract in a study using silymarin aqueous and ethanolic extracts in a modified forced swimming test, indicating an antidepressant effect. The ethanolic extract, however, did not have such a result. This suggests that silymarin may have the ability to regulate neurotransmitter levels and enhance mood.

Conclusion

In conclusion, milk thistle is a complex plant that has attracted a lot of interest lately because of its wide range of phytochemicals and potential pharmacological effects. Milk thistle is a well-liked option for people looking for natural therapies for liver problems and detoxification because the main active ingredient, silymarin, has been thoroughly studied for its hepatoprotective and antioxidant benefits. Additionally, its anti-inflammatory and anticancer properties have expanded its range of possible medicinal uses.Although milk thistle has been used traditionally for hundreds of years, there is now compelling scientific evidence that it is useful for a wide range of medical issues. To clarify its mechanisms of action and investigate its potential in treating a wider spectrum of medical problems, more research is nonetheless required. Milk thistle is a promising plant with a lot of unrealized potential as the desire for natural and holistic approaches to treatment rises.It is crucial to carry out thorough clinical trials and long-term investigations to establish milk thistle's safety and efficacy as we continue to understand the complex interactions between the phytochemicals in milk thistle and the human body. Milk thistle may become a more significant component of integrative medicine by bridging the gap between conventional wisdom and modern research, opening up new opportunities for enhancing health and wellbeing.

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