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Review

Exploring the potential of silymarin in agriculture: A review

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Abstract: Silymarin, a bioactive compound derived primarily from the seeds and fruit of the milk thistle (*Silybum marianum*) plant, has garnered increasing attention in recent years due to its potential applications in agriculture. This comprehensive review explores the multifaceted role of silymarin in agricultural practices, shedding light on its chemistry, biological activities, and diverse applications. The chemical structure and properties of silymarin are elucidated, emphasizing its unique solubility, stability, and bioavailability, which render it suitable for agricultural use. A significant portion of the review is dedicated to examining the biological activities of silymarin, which encompasses its antioxidant properties. The underlying mechanisms responsible for these activities are explored, highlighting their potential as a natural solution for mitigating environmental stressors that adversely affect crop health and productivity. Illustrative examples from research studies and practical applications underscore its effectiveness in safeguarding agricultural yields and ensuring food security. Furthermore, the review delves into the potential of silymarin to enhance crop growth, yield, and quality. Mechanisms through which silymarin influences plant physiology and metabolism are examined, providing valuable insights into its role as a growth-promoting agent in agriculture. The review concludes with a forward-looking examination of the prospects of silymarin in agriculture, highlighting emerging trends and areas of innovation that hold promise for sustainable and resilient farming systems. In summary, this review consolidates the current body of knowledge surrounding silymarin's potential in agriculture. It underscores the versatility of silymarin as a natural tool for crop protection, growth enhancement, and environmental sustainability, offering valuable insights for researchers, practitioners, and policymakers seeking innovative approaches to address the challenges of modern agriculture.

Keywords: silymarin; agriculture; crop protection; antioxidant; plant growth; sustainable farming; environmental stress

1. Introduction

The search for innovative and sustainable solutions in agriculture has led to the exploration of bioactive compounds with the potential to revolutionize farming practices [1–11]. Among these compounds, silymarin, an intriguing phytochemical, has emerged as a subject of growing interest. Silymarin finds its origins in the seeds and fruit of the milk thistle plant (*Silybum marianum*), a spiky-leaved herbaceous plant native to the Mediterranean region [12]. Milk thistle, with its vibrant purple flowers and distinctive white-veined leaves, has a long history of use in traditional medicine and has been recognized for its hepatoprotective properties for centuries [13]. It is in the seeds of this ancient plant that silymarin is most abundantly found. Comprising a complex mixture of flavonolignans, including silybin, silydianin, and silychristin, silymarin has gained renown not only for its therapeutic potential in human medicine but also for its multifaceted utility in agriculture [14].

In this comprehensive review, we delve into the multifaceted role of silymarin in agricultural practices, offering a glimpse into its chemical composition, properties, and diverse applications. As the global agricultural landscape faces increasing challenges, including pest pressures, climate variability, and the need for sustainable farming practices, silymarin emerges as a promising candidate for addressing these issues [15–21]. Its unique attributes, both in terms of its chemistry and biological activities, make it a compelling subject for exploration in the context of modern agriculture. This review embarks on a journey through the realms of silymarin's potential in agriculture, shedding light on its sources, biological activities, applications in crop protection, and its capacity to enhance crop growth and yield. Additionally, we consider the environmental implications and challenges associated with its use, providing a balanced perspective on its role in fostering sustainable agricultural systems. In the following sections, we will navigate through the intricate web of knowledge surrounding silymarin's agricultural applications, ultimately aiming to provide valuable insights for researchers, practitioners, and policymakers seeking innovative approaches to advance the field of agriculture.

2. Origin, chemistry, and properties of silymarin

Silymarin (SM), the bioactive complex derived from milk thistle (*Silybum marianum*), stands out for its intricate chemistry and a host of unique properties that make it a versatile candidate for various agricultural applications. SM is a flavonolignan extracted from the seeds or fruits of the *Silybum marianum* plant [14,22]. *S. marianum* is an annual or biennial herbaceous medicinal plant. It is a tall herb up to 2 meters high with large leaves, hard spikes and tubular flowers. The plant derives its name due to the presence of milky veins on the leaves [23]. It belongs to the largest and widespread family (*Asteraceae*), with the English name of milk thistle or Mary's thistle [24,25]. *S. marianum* includes two varieties, a less abundant variety Albiflorum with white corollas and a more abundant variety Purple with purple corollas, and the thorns are found on all aerial parts of the plant [26,27]. Fruit yield of milk thistle ranges 550–1680 kg/ha and silymarin production ranges 13.30–35.40 kg/ha [28]. This plant is widespread worldwide and grown for centuries throughout Europe, Africa, China, India, Australia, and the Mediterranean region. It is known as Shook Elgamal in Egypt [29,30]. For over 2000 years, milk thistle plant has been regarded as one of the important medicinal plants. The whole plant is used as animal feed, seed oil, besides culinary uses and it can be utilized for biodiesel or polymer production [29]. And it is used as a vegetable, as salad, as bitter tonic, and as galactogogue in nursing mothers and in various ailments such as liver complications, depression, dyspepsia, spleenic congestions, varicose veins, diabetes, amenorrhea, uterine hemorrhage, and menstrual problems [31]. It has been a common formulation used in Asian clinics since the 1200s [32]. And its marketing of the use of for medical purposes has been emerged since the 1970s. It is among the top-selling products in US, Italy and in other countries [33].

Understanding the chemical composition and inherent properties of silymarin is fundamental to appreciate its potential in agriculture. The active constituent of *S. marianum* is silymarin, which is a C-25 containing flavonolignan. The standardized extract contains approximately 65–80 % of flavonolignans, i.e. silybin A and silybin

B, isosilybin A, isosilybin B, silychristin and silydianin, small amounts of flavonoids, and 20–30 % of fatty acids, betaine, apigenin, silybonol, proteins, fixed oil, and polyphenolic compounds [14,31]. With an empirical formula $C_{25}H_{22}O_{10}$ [13]. Among these chemical constituents, silybin is the biological active component. Silybin is a mixture of two diastereomers A and B in approximately 1:1 proportion [31]. Costanzo and Angelico [34] and Surai [14] mentioned that, silymarin is primarily composed of a group of flavonolignans, with silybin or silibinin (33.4%), silydianin (3.5%), silychristin (12.9%), and isosilybin (8.35%) being the principal constituents. These flavonolignans are polyphenolic compounds characterized by their distinctive chemical structure, which includes a flavonoid moiety combined with a lignan-like structure. This chemical complexity contributes to the compound's diverse biological activities.

Silymarin exhibits a relatively low water solubility, which can present challenges in its application. However, its lipophilic nature allows it to dissolve readily in organic solvents, making it amenable to various formulation techniques. Strategies to enhance its solubility, such as the development of nano emulsions and encapsulation technologies, have been explored to improve its delivery and efficacy in agriculture [34]. Silymarin is known to be sensitive to environmental factors such as heat, light, and oxygen. Proper storage conditions, including protection from direct sunlight and excessive moisture, are essential to maintain its efficacy over time [35]. Formulation approaches that enhance stability are essential for practical agricultural use. One of the most remarkable aspects of silymarin is its wide range of biological activities. It is renowned for its potent antioxidant properties, which stem from its ability to scavenge free radicals and protect cellular components from oxidative damage [36–38]. Additionally, silymarin exhibits anti-inflammatory effects and is recognized for its hepatoprotective capabilities in mammals [13].

Silymarin's diverse biological activities are mediated through various mechanisms. Its antioxidant effects involve the inhibition of reactive oxygen species (ROS) and the enhancement of endogenous antioxidant systems [14,39]. The antioxidant effects are attributed to the biotransformation of silybin diastereomers, resulting in the creation of glucuronide derivatives (**Figure 1**). Moreover, it exerts anti-inflammatory effects by modulating cytokine production and inhibiting inflammatory pathways [40]. These mechanisms are integral to its potential applications in agriculture, where oxidative stress can adversely affect crops. Understanding the chemistry and properties of silymarin provides a solid foundation for exploring its applications in agriculture. Despite its challenges related to solubility and stability, its unique chemical structure and biological activities make it a promising candidate for addressing the evolving needs of modern farming practices. In the subsequent sections of this review, we will delve into the practical implications of these properties, exploring how silymarin can be harnessed to enhance crop protection, growth, and overall agricultural sustainability.

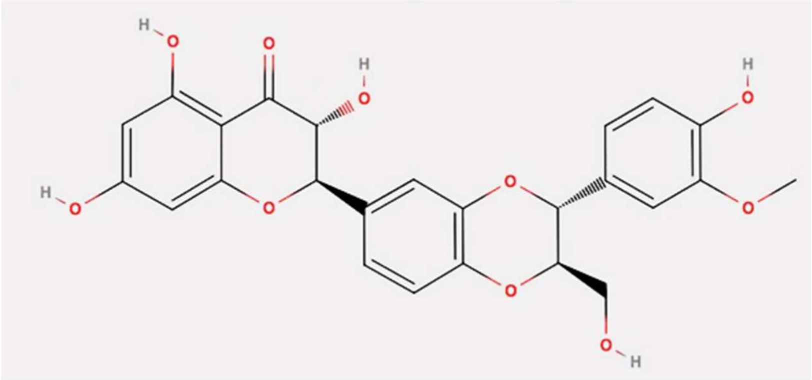

Figure 1. Chemical structure of silybin.

3. Typical applications of silymarin

Silymarin has been used medicinally to treat liver disorder, including acute and chronic viral hepatitis, toxin/drug-induced hepatitis and cirrhosis and alcoholic liver diseases [12,24]. And other list of diseases such as anorexia disease, cancer disease, demulcent in catarrh and pleurisy, diabete estrogen-related diseases, hemorrhoids, hydrophaints, malaria, and spleen disease [30]. Also cardioprotective effects of silymarin is reported on chemotherapeutics such as doxorubicin and cisplatin [41]. And inflammatory disorders, renal disorders, skin disorders, lung disorders, and many more [31]. And also protecting the brain from the inflammatory and oxidative stress effects by which metabolic syndrome contributes to neurodegenerative diseases [34].

Medical and pharmacological studies on humans and animals have confirmed the antioxidant effect of silymarin in the prevention and treatment of the aforementioned diseases. Most studies have agreed that SM can contribute to the antioxidant defenses in different ways. Firstly, by direct free radical scavenging. Secondly, by preventing free radical formation by inhibiting specific enzymes responsible for free radical production, or by maintaining the integrity of electron-transport chain of mitochondria in stress conditions. Thirdly, by participating in the maintenance of optimal redox status of the cell by activating a range of antioxidant enzymes and non-enzymatic antioxidants, and providing additional protection in stress conditions [13,14,32,37,38,41,42]. Silymarin has activity against lipid peroxidation as a result of free radical scavenging and the ability to increase the cellular content of glutathione GSH, ability to regulate the membrane permeability and to increase membrane stability, and capacity to regulate the nuclear expression [22,37,38]. It has been reported that silibinin is a powerful iron chelator, thereby inhibiting the oxidation of linoleic acid catalyzed by $Fe2+$ salts [43]. Silymarin maintains the normal membrane fluidity by directly interacting with cell membrane components, thereby preventing alteration in the content of lipid fraction [44,45].

Both animal and human studies showed that silymarin is nontoxic even when given at high doses (>1500 mg/day), but the main drawback of silymarin is its poor solubility (<50 µg/mL) therefore different approaches are been taken to enhance the solubility [13]. The use of nanotechnological strategies appears to be a promising method to enhance sustained release of the active herbal extract [34].

4. The agricultural applications of silymarin

The potential for high yields and the diverse chemical composition of milk thistle fruits and vegetative biomass have opened the door to a wide range of potential applications of silymarin (**Table 1**). These applications span from livestock nutrition to human dietary use and industrial applications, encompassing various plant components, derivatives, and extracts [14–16,19,20,46,47].

Table 1. Summary of selected recently reported studies utilizing silymarin to enhance plant growth and resistance to biotic and abiotic stresses.

Method and rate of silymarin application	Study objectives	Outcomes	Reference
• Foliar application on Cd-Stressed **wheat** • 0.5 mM silymarin	• Morphological, biochemical, and physiological	• ↑ Growth, and productivity, total chlorophylls, total carotenoids, *Pn*, Tr, *Gs*, RWC, and MSI. • ↑ POX, CAT, SOD, AsA, α-TOC, and GSH. • ↓ EL, MDA, H_2O_2, and $O^{\bullet-}_2$	[19]
• Seed soaking + foliar application on Cd-Stressed **wheat** • 0.5 mM silymarin	• Morphological, biochemical, and physiological	• ↑ photosynthesis pigments. • ↑ proline, AsA, GSH, Sim, SOD, CAT, APX, and GR. • ↓ EL, MDA, H_2O_2, Cd_2, and $O^{\bullet-}_2$	[17]
• Seed priming + foliar application on Cd-Stressed ***Phaseolus vulgaris*** • 250 µM silymarin	• Morphological, biochemical, and physiological	• ↑ Enzymatic and non-enzymatic antioxidants and osmolyte accumulations. • ↑ Endogenous polyamine (Put, Spd, and Spm) and polyamine metabolic enzyme (ADC and ODC) activities. • ↓ Minimizing ROS accumulation	[15]
• Foliar application on Cd-Stressed **maize** • 0.5 mM silymarin	• Morphological, biochemical, and physiological	• ↑ plant growth and biomass accumulation. • ↑ photosynthesis efficiency, enzymatic and nonenzymatic antioxidants, antioxidant redox state, hormonal content and homeostasis, and enzyme gene expression. • ↓ lipid peroxidation, ionic leakage, and oxidative damage catalyzed by ROSs ($O^{\bullet-}_2$ and H_2O_2)	[16]
• Foliar application on **rice** • 10, 25, 50, 125, 250, 500, 1000 and 2000 mg silymarin /L	• Systemic acquired resistance (SAR) against rice blast disease	• ↑ Inducing resistance to rice blast disease.	[20]
• Foliar application on ***Atriplex nummularia*** under saline-calcareous stress • 200 µg silymarin /L	• Morphological, biochemical, and physiological	• ↑ Plant tolerance, and enhanced *Atriplex nummularia* seedling productivity.	[21]

Pn: leaf net photosynthetic rate, Tr: rate of transpiration, gs: stomatal conductance, RWC: relative water content, MSI: membrane stability index, POX: peroxidase, CAT: catalase, SOD: superoxide dismutase, AsA: ascorbate (AsA), α-TOC: alpha-tocopherol, GSH: glutathione, EL: Electrolyte leakage, MDA: malondialdehyde, H_2O_2: hydrogen peroxide, $O^{\bullet-}_2$: superoxide radical, Put: putrescine, Spd: spermidine, Spm: spermine, ADC: arginine decarboxylases, ODC: ornithine decarboxylases, ROS: reactive oxygen species.

Drought stress enhanced the accumulation of silymarin in milk thistle seeds and improved its quality by increasing the share of silybin, which possess the greatest degree of biological activity among the silymarin components. it seems that enhancement of silymarin accumulation in milk thistle seeds is part of the defense mechanism of this plant against drought stress which helps milk thistle to tolerate the stressful condition for a longer period of time [48].

Exogenously-applied honey bee enriched with silymarin effectively attenuated salinity (10 dS m^{-1}) stress damage to the chili pepper plant growth, physiological, and yield attributes through the increase in K^+/Na^+ ratio, non-enzymatic antioxidant, and osmoprotectant levels, enzymatic antioxidant activities, hormonal contents, and gene expressions along with decreased Na^+ and Cl^- contents, oxidative stress markers, and ABA levels, and oxidative stress-related membrane damage [36]. Silymarin was used as a systemic acquired resistance (SAR) substance in rice (*Oryza sativa* L.) against rice blast disease caused by *Magnaporthe oryzae*. The results pointed to the role of silymarin in inducing resistance to rice blast disease. Significant improvement of resistance under greenhouse conditions with different concentrations 10, 25, 50, 125, 250, 500, 1000 and 2000 mg/L of silymarin was recorded. The most suitable concentration was 500 mg/L. The recorded disease severity was 23.5% when applied five days before inoculation and significantly reduced disease severity under field condition at both experimental seasons [20].

On the other hand, silymarin was found to improve the growth and biomass accumulation of maize plants under cadmium (Cd) stress conditions. This enhancement encompassed various aspects, including increased growth, improved photosynthesis efficiency, heightened levels of non-enzymatic antioxidants, maintenance of antioxidant redox balance, regulation of hormonal content, and homeostasis. Additionally, the application of silymarin via foliar spraying resulted in elevated enzymatic antioxidants and influenced the expression of relevant enzyme genes. Most notably, this treatment effectively mitigated lipid peroxidation, reduced ionic leakage, and protected against oxidative damage catalyzed by reactive oxygen species (ROS) [16]. These positive outcomes were attributed to the inhibition of Cd ion buildup and the activation of antioxidant defense mechanisms in maize plants under Cd-induced stress. Notably, this study revealed that the beneficial effects of silymarin were even more pronounced in the presence of Cd stress compared to normal conditions. The application of silymarin through foliar application improved both the growth of wheat plants and their biomass accumulation in the presence of Cd-induced stress [19]. Silymarin's antioxidant properties contributed to enhanced growth, increased photosynthetic efficiency, and the bolstering of both nonenzymatic and enzymatic antioxidant systems. Consequently, this led to a reduction in oxidative damage inflicted by reactive oxygen species ($O_2^{\bullet-}$ and H_2O_2), ionic leakage, and lipid peroxidation. These findings were primarily attributable to the restriction of Cd ion accumulation and the concurrent activation of antioxidant defenses in wheat plants subjected to Cd-induced stress. The external application of silymarin significantly bolstered common bean plants' ability to withstand cadmium-induced damage. This protective effect was achieved by reducing the accumulation of reactive oxygen species (ROS), enhancing both enzymatic and non-enzymatic antioxidants, and increasing osmolyte levels. These measures collectively served to preserve the integrity of cell membranes under stress conditions. Moreover, the heightened levels of endogenous polyamines (Putrescine, Spermidine, and Spermine) and the increased activities of polyamine metabolic enzymes (Arginine Decarboxylase and Ornithine Decarboxylase), influenced by silymarin, emerged as pivotal factors in fortifying common bean plants against cadmium-induced damage [15].

5. Conclusion

In a world where agriculture grapples with a growing set of challenges, from environmental stressors to the demand for sustainable practices, silymarin emerges as a captivating agent of change. This comprehensive review has explored the multifaceted role of silymarin in the realm of agriculture, illuminating its potential as an innovative and sustainable solution. Derived primarily from the seeds and fruit of the milk thistle plant, silymarin offers unique attributes, from its intricate chemistry to its versatile biological activities. Its antioxidant properties, rooted in the ability to combat free radicals and protect against oxidative stress, make it an exceptional candidate for addressing the myriad challenges facing crop health and productivity. It is in this context that silymarin's agricultural applications shine with promise. Our exploration has unveiled its capacity to serve as a natural shield against pests, diseases, and abiotic stressors that jeopardize crop yields. It is not limited to theory; real-world studies and practical applications have demonstrated its efficacy in safeguarding agricultural outputs. Additionally, silymarin's potential to bolster crop growth, yield, and quality serves as a beacon of hope for enhancing agricultural productivity. What sets silymarin apart is its versatility, as it finds applications in diverse agricultural settings. From organic farming systems to controlled-environment agriculture, its role in protecting crops and promoting growth is indispensable. The evidence is clear: silymarin is not only a growth-promoting agent but also a shield against agricultural adversity. As agriculture looks to balance productivity with sustainability, silymarin's entry into the field is timely. Its potential to reduce dependence on synthetic chemicals and enhance food safety makes it a compelling solution. By mitigating oxidative stress, preserving soil health, and contributing to sustainable agricultural practices, silymarin holds the promise of a brighter, more resilient, and environmentally conscious future for farming. In conclusion, this review consolidates the ever-growing body of knowledge surrounding silymarin's pivotal role in agriculture. Its capacity to protect crops, enhance growth, and promote environmental sustainability is a beacon of hope in the face of contemporary agricultural challenges. For researchers and practitioners, silymarin stands as a promising ally in the quest for innovative and sustainable farming solutions, ultimately contributing to food security and a more resilient agricultural future.

Conflict of interest: The authors declare no conflict of interest.

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