Study of General and Cultivation Characteristics of Silybum Marianum and Its Importance in Human Diseases, Biotechnology and Pharmacological Activities: A Review

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ABSTRACT

Silibum Marianum, which is known as milk is widely used in traditional medicine for its therapeutic properties. It has shown that the main component of the Selipine belongs to a group of flavonoids called Flavonoliganz, known as its antioxidant and anti-inflammatory impacts, and the cellippine has been characterized by its unique buildings Accordingly, Silibum Marianum shows promising potential in enhancing cardiovascular health by making cholesterol levels, hazarding the composition of bridges, and the exercise of antioxidant and anti-inflammatory procedures These characteristics and their features are antioxidants, they do so play a crucial role in protecting cells from damage caused by oxidative and discrepancies in chronic diseases such as cancer, diabetes and nervous degeneration disorders and research suggested In addition, investigations explored its potential anti-cancer properties, including inhibition of cancer cell proliferation, incitement of the death of programmed cells, and mitigate side effects of chemotherapy. In essence, Silibum Marianum, is introduced by Silippians as the active biological component, a range of potential health benefits ranging from liver support to cardiovascular protection and antioxidants effects.

Keyword: *Silybum marianum; henylpropanoid; neurodegenerative disorders; anti-inflammatory*

INTRODUCTION

According to Khatri et al. (2022), the milk thorn plant, also known as Silybum Marianum L. Gaertn, has gained a lot of popularity and has been utilized in traditional medicine due to its promise in the treatment of liver and stomach problems. In addition to possessing several preventative capabilities of the liver, he is well-known for the fact that it is shielded from the potentially damaging effects of alcohol, medications, and environmental contaminants. According to Sõukand et al. (2017), it has been demonstrated that the milk plant has been planted across Europe for the purpose of harvesting its numerous components, such as roots, flowers, leaves, and roasted fruits. These parts were utilized as a nutritious source of food for both humans and cattle. In addition, many regions have been embellished by one of its applications, which is thriving, notably flourishing in various kinds of soil. Other locations have been adorned accordingly. In the early records of physicians and healers, as well as in the ancient pamphlets, there is evidence of their investigation and reporting of the medical advantages of milk. (2015) According to Akhtar et al. Additional flavonolignans, such as isosilybin, silychristin, and silydianin, are found in milk thistle fruits in different concentrations, in addition to silymarin, which is only found in milk thistle fruits. According to Mihajlovic et al. (2023), milk thistle fruits contain a high concentration of fatty acids, protein, tocopherols, sterols, and other beneficial compounds. Three-deoxyflavonolignan and mucilage are two examples of this kind of chemicals. Silymarin, which is a component of one of the flavonolignan complexes, is the primary candidate for the therapeutic characteristics that it possesses, according to our findings. 1968 was the year when silymarin was first extracted from the fruits of the milk thistle plant, which are known as achenes. The silybin, which is often referred to as silibinin, is the primary component of silymarin oil. The purpose of this study is to promote a correct knowledge of the therapeutic qualities of milk thistle and its prospective uses in the treatment of liver and gallbladder problems, as stated by Anthony et al. (2013). It is possible to identify the active ingredients

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responsible for its effects according to each part of the body, which would provide clarifications about the fundamental mechanisms of action. Although its benefits are recognized in traditional medicine, there is a great deal more scientific research that needs to be done in order to verify its effectiveness. According to Wianowska et al. (2014)

One of the primary objectives is to delve more deeply into the chemical and biological characteristics of milk thistle. Additionally, we always do research on the possible beneficial effects that milk thistle may have on the liver and therapeutic applications when the liver's functions are disrupted. This may be accomplished by conducting a thorough investigation of the constituents and methods of action of milk thistle. By doing so, we will get a deeper comprehension of the pharmacological capabilities of milk thistle and locate areas that show promise for therapeutic use.

The process of understanding and therapeutic mechanisms helps in achieving highly reliable and continuous treatment results for liver and gallbladder disorders (Asrani, et al., 2019). Therefore, one of the necessities of research within its field is to ensure maximum effectiveness and safety within its study processes. This is done in order to reduce the gaps that occur within its study processes.

REVIEW OF LITERATURE

Scientific Name and Common Names

The scientific name for this plant is Silybum marianum (L.) Gaertn, which is a synonym for Carduus marianum L. (DOÞAN, et al, 2022). However, it is known by a variety of other names. Holy Thistle, Mary's Thistle, Saint Mary's Thistle, Mary's Thistle, Our Lady's Thistle, Christ's Crown, Rose Thistle, Healing Thistle, Miscellaneous Thistle, Hog Leaf, Royal Thistle, Serpent's Milk Thistle, Sow Thistle, and Wild Artichoke are some of the names that are used to refer to these plants. Furthermore, its names are assigned according to the locations in which it is commonly found, which results in a wide range of names being used to refer to it. 2014 study by Hamouda et al. Just one example:

- Within the Persian language, he is called Maryam Thaqal or Khar Maryam.
- In Arabic, it is called Al-Aqoub, Shouk Al-Diman, Shouk Al-Nasara, or Harshav Beri.
- In French it is called Chardon-Marie, Chardon argente or Artichaut sauvage.
- It is known as Mariendistel in German
- In the Chinese language, it is called Shui Fei Ji.
- In Spanish, it is called Cardo Mariano or Cardo Lechero, depending on the province.

The process of understanding the different names of the plant associated with milk thistle confirms its recognition and uses across different cultures and regions throughout history where the botanical name Silybum marianum indicates the historical antiquity in the field of use and mythology surrounding the plant. “Silybum” refers to the edible thorns described by Dioscorides, an ancient Greek physician and botanist (Asrani, et al, 2019).

The specific term “marinium” indicates that the white veins on the plant’s leaves were caused by a drop of the Virgin Mary’s milk (Abenavoli, et al, 2010). According to some accounts and in pharmacopoeias, the practical name of the milk thistle plant is called Cardui mariae fructus(**Student, et al, 2013**)

Taxonomy

Classification helps scientists and researchers classify and compare different species. Understanding the specific classification of milk thistle is crucial because it provides a uniform and systematic approach to identifying and studying the plant while understanding its evolutionary relationships, and investigating its ecological and medicinal properties (Radek et al, 2007). marianum according to the hierarchy via:

- Superdivision: Spermatophytes, including seed plants that reproduce by producing seeds.
- The Kingdom: Plants, which includes all plants.
- Sub-kingdom: Tracheobionta, representing vascular plants with specialized tissues for transporting water and nutrients.
- Section: Magnoleophyta, which includes flowering plants.
- Class: Magnoliopsida, composed of dicots or dicots characterized by a set of embryos with two cotyledons or seed leaves (Wianowska et al., 2014).
- Researchers are able to arrange and analyze milk thistle and its plants in a manner that is really clinical if they adhere to this agreed-upon system of plant categorization (Porwal, et al, 2019).

Asteridae is the subfamily that is utilized for classification. This subfamily is comprised of plants that have blooms that frequently have united petals, which gives them a tubular or ovate form. The botanical order known as Asteraceae is comprised of many families of blooming plants. According to Radek et al.'s 2007 research, milk thistle is a plant that belongs to the Asteraceae family, which is also referred to as the other family. The Asteraceae family is a huge and diversified family that includes various species that are well-known for their flower heads that are organized in a cluster. According to the classification of botanist Michel Adanson, the genus is defined as Silybum (Serce, et al, 2016).

ECOLOGY

T The high value and exceptional advantage is the ability of the milk thistle plant (Silybum marianum) to adapt to diverse environmental conditions. This is the reason for its successful growth in different environments and climates from northern regions such as Canada to arid southern regions. Therefore, it is said that this diversity makes it a versatile choice. Uses in agriculture (Radek et al., 2007).

Silybin content is higher in subtropical regions, according to studies, and it is the main component of silymarin. Therefore, we conclude that high temperatures enhance the accumulation of silybin. Here we reach another conclusion, which is that geographical and climatic conditions greatly affect the silymarin content in milk thistle fruits (Hobbs, 2008).

Regarding soil type, it has been shown that milk thistle has strong growth and high productivity across various soil types, although it is often considered a weed in undesirable locations such as roadsides and wastelands, as this is explained by its ability to compete with crops for water. and nutrients (Teo et al., 2008).

Numerous studies show that this plant thrives in high-nitrogen environments including dairy yards, chicken manure, landfills, and abandoned agricultural fields (Huie et al., 2002).

The ability of the plant to adapt to diverse climates, its ability to grow in different types of soil, and the diversity in silymarin content based on environmental conditions contribute to its environmental and agricultural importance. It is very important because it is a reason for understanding the characteristics of this plant and therefore they are of high importance in treating diseases that affect humans and exploring its biotechnological and pharmaceutical activities (Serce et al., 2016)

THE MOST IMPORTANT MEDICINAL PROPERTIES OF THE PLANT IN TREATING VARIOUS DISEASES

Its importance in treating many diseases is due to it containing silymarin, which is considered one of the main active compounds effective in maintaining liver health (Saler, 2001).

Silymarin works as a first line of defense for the liver against harmful substances such as (toxins, alcohol, and some medications), as it stimulates the regeneration process of liver cells and facilitates the detoxification process, meaning that its function here is to give the liver flexibility in regeneration and resistance (Hobbs, 2008).

Its other importance is in fighting infections because it acts as an antioxidant and thus combats many chronic diseases. (Wianowska et al., 2014).

Studies have also shown effects on cholesterol levels, as it reduces LDL (bad cholesterol) and increases HDL (good cholesterol), which is beneficial in improving cardiovascular flexibility (Teo et al., 2008).

It has been shown that this plant has the ability to control blood sugar levels and enhance insulin sensitivity. (Radek, et al., 2007)

The extracts of this plant have great effectiveness in treating many skin diseases, according to what many studies have shown, and an example of these skin diseases is acne, psoriasis, and eczema, through the therapeutic antioxidant and anti-inflammatory mechanisms found in milk thistle to soothe and heal the skin (Asrani et al., 2019).

This confirms the process of continuous research and discovery on this subject in order to achieve the full multiple benefits that treat multiple diseases through milk thistle.

THE HEPATOPROTECTIVE POWER OF SILYMARIN IN MILK THISTLE SEED

It is clear to us that this plant contains a large group of biologically distinct elements, and most of these elements are located within milk thistle seeds (Serce et al., 2016).

Among these important biological compounds are apigenin, silybin, and silymarin, and all of these elements are compounds that have very important health effects and affect the human body in various organs (Drouet, et al, 2018).

Silymarin, which is known as a compound consisting of a mixture of flavonoids found abundantly in milk thistle seeds, has a beneficial therapeutic nature that affects liver health (Asrani, et al, 2019). Through multiple studies, it has been shown that this compound works to inhibit liver toxicity and stop Liver cirrhosis and the treatment of all types of viral hepatitis, and therefore it has great benefit for treating various and diverse liver disorders (Radic et al., 2007).

Its mechanism is by enhancing effective absorption from the digestive system by working to deliver positive elements to the desired areas within the body (Younas, et al., 2018). That is, it protects liver cells from harmful oxidative stress that causes liver damage while liberating free radicals. It works to Stopping it and thus maintaining liver function and health. In general (Taleb et al., 2013).

It ensures effective absorption from the digestive tract and targeted delivery to desired areas of the body (Yonas et al., 2018). Its properties play pivotal role in protecting liver cells from oxidative stress and harmful effects of free radicals, thus maintaining liver function and overall health (Student et al., 2013).

By neutralizing reactive oxygen species, silymarin protects the cell walls and thus prevents inflammation from reaching the liver cells, thus preventing the occurrence of hepatitis and improving the damaged cell within it (Asrani et al., 2019).

As for the detoxification mechanism, silymarin facilitates the passage and flow of bile to the liver and thus cleanses the liver periodically (Teo et al., 2008). Its protective effects extend to the kidneys, where it prevents the toxic effects of various chemicals and medications, reduces the risk of viral liver diseases, and mitigates associated tissue damage (Wianowska et al., 2014).

Due to its antioxidant efficacy and hepatoprotective effects, silymarin shows promise as a potential therapeutic agent for liver and kidney diseases, toxin poisoning, and certain types of cancer (Yunus et al., 2018).

Compound Antioxidant Properties

It revealed great benefits in protecting cells from oxidative stress, as the effect of silymarin on the activity of the antioxidant enzyme was shown, while it works to reduce fat decomposition on a large scale and thus has a high contribution to reducing disease and aging (Jaafar et al., 2024).

Oxidative stress arises when the body's balance between antioxidants and free radicals is disturbed, which are characterized by unstable molecules with unpaired electrons, inciting damage to DNA, proteins, and fats within the body (Saler, 2001).

Silymarin's antioxidant properties counteract the damaging effects of free radicals, increasing the activity of vital antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) (Banaee, et al., 2023).

This enhancement enhances the body's ability to fight oxidation and maintain its innate homeostasis (Hong, et al, 2015). In addition, silymarin limits lipolysis, a process implicated in cell membrane damage and the formation of harmful compounds known as lipid peroxides (Teo et al., 2008).

By attenuating lipolysis, silymarin maintains cellular membrane integrity, improves cellular function, and appears as a formidable defender against cellular damage caused by free radicals. Research suggests its potential effectiveness in preventing and treating various diseases associated with oxidative stress, including cardiovascular disease and cancer (Subramaniam et al., 2007).

Anti-inflammatory properties

Silymarin exhibits remarkable features, according to its action as an inflammatory shield by targeting the transcription factor NF-κB, which is a master regulator responsible for coordinating the expression of genes involved in inflammation and cell survival. Its principles are through the inhibition of NF-κB, and thus silymarin

will effectively reduce the inflammatory response in the body and thus provide relief after Conditions characterized by chronic inflammation (Malikzadeh et al., 2013).

The other principle, by modulating the activity of NF-κB, silymarin offers a promising way to treat a range of inflammatory disorders. By disrupting the complex molecular pathways that cause inflammation, silymarin emerges as a natural ally in alleviating inflammatory attacks on the body's tissues and organs (Saupe, et al., 2022).

Incorporating silymarin-rich sources such as milk thistle seed into the diet or nutritional supplement regimen may provide a natural way to manage inflammation and promote overall health (Soysal, 2009).

Treatment mechanisms:

Silymarin has received much attention for its diverse therapeutic properties. This part of the study investigated the effectiveness of this plant in treating poisoning due to the Amanita mushroom, in addition to its anti-cancer activities and its important role in diabetes management (Asrani, et al, 2019).

1. Silymarin in treating Amanita mushroom poisoning:

Amanita mushrooms pose a high risk because they contain many liver toxins, such as alpha-amanitin. Therefore, this type poses great harm because it quickly damages the liver and thus will lead to death (Müller, et al., 2001).

It has been shown that silymarin has therapeutic efficacy by reducing or preventing infection through mechanisms. Different ways to prevent liver damage according to:

1. Its active antioxidant activity: As mentioned in studies (Asrani et al., 2019), silymarin acts as an antioxidant according to a mechanism that neutralizes harmful free radicals resulting from the process of liver toxicity according to a process that reduces oxidative stress or prevents subsequent liver damage by eliminating of reactive oxygen species (ROS) and preventing lipid peroxidation (Sears et al., 2016).
2. The mechanism of inhibiting critical inflammatory pathways: It inhibits cytokines and mediators that cause inflammation such as tumor necrosis factor alpha (TNF-α) and nuclear factor kappa B (NF-κB), which are pivotal in the inflammatory response associated with mushroom poisoning. This inhibition helps reduce inflammation. Protecting liver cells from further damage, even in subsequent relapsing or reversible cases (Asrani et al., 2019)
3. The ability to enhance liver cell regeneration: Silymarin has the ability to regenerate liver cells by stimulating protein synthesis and periodically promoting the formation of new liver cells. This mechanism carries out an extensive restoration and repair process within damaged liver tissue, which helps and accelerates recovery from liver injury caused by fungi (Mani et al., 2007),

Through these mechanisms, it has been shown that silymarin plays a crucial role in preventing or reducing liver damage caused by Amanita mushroom poisoning, thus confirming the effectiveness of silymarin found in milk thistle..

2. Anticancer activity of silymarin:

Silybin works to combat various types of cancer (Asrani, et al., 2019), as the mechanisms by which silymarin works and its anti-cancer effects are according to the following:

- Silymarin effectively inhibits cell survival pathways such as the phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) pathway, which are often abnormal and therefore dysregulated within cancer cells ,This inhibition leads to reduced cell proliferation and increased sensitivity to apoptotic signals. (Mani et al., 2007).
- Silymarin stimulates programmed cell death, known as apoptosis, in cancer cells. It activates caspases, which are enzymes responsible for initiating and executing the apoptotic process, leading to the death of cancer cells. Silymarin inhibits the growth of cancer cells by interfering with cell cycle progression, arresting cells in the G1 phase, and preventing uncontrolled proliferation (Müller, et al., 2001).
- Antiangiogenic effects that support tumors: Silymarin prevents angiogenesis, the formation of new blood vessels that support tumor growth. It inhibits the production of vascular endothelial growth factor (VEGF) and other pro-angiogenic factors, thus limiting blood flow to tumors (Mani et al., 2007).

3. Silymarin and Diabetes Management:

Silymarin helps reduce fasting blood sugar levels and improves insulin sensitivity. It has shown potential in diabetes management by exerting antidiabetic effects because it enhances insulin management by:

Stimulate insulin secretion from pancreatic beta cells and this in turn will improve glucose metabolism and lower blood glucose levels (Asrani, et al, 2019).

This will also prompt silymarin to uptake glucose by skeletal muscle cells and adipocytes, which enhances glucose utilization and reduces high levels of glucose. Blood sugar and thus silymarin exhibits protective effects on pancreatic beta cells and thus maintains their function and ability to survive. (Serce, et al, 2016).

The history of the hypoglycemic effects of silymarin includes:

1. Stimulate the secretion of diabetes: The examination indicates that silymarin can stimulate beta cell secretion obviously, leading to the reversal of blood sugar lines. This helps to regulate sugar levels in the body (Muller, et al, 2001).

2. Increased absorption by the body: Silymarin is rapidly produced by skeletal cells and cytolytic cells, which increases its effect on blood sugar levels. This is limited to improving the body's ability to use everything efficiently (Soysal, 2009).

3. Protection against visible beta cell damage: Silymarin exhibits protective effects on beta cells other than ensuring their ability to survive. In order to eliminate food and infections in the body and also prevent beta cell damage and disorders (Asrani, et al, 2019).

Hence, the therapeutic and preventive principles here are to exceptionally strengthen and protect beta cells. These effects can lead to low blood sugar volume, which reduces diabetes management. However, the doctor should note that there may be some people who take silymarin, and they must use it as part of physical therapy (Muller, et al, 2001).

4. Mechanism of treatment against inflammation:

Silymarin has good anti-inflammatory properties as it modulates the transcription factor NF-κB, which leads to reducing inflammation according to the following mechanisms:

a. NF-κB inhibition:

NF-κB, a pivotal transcription factor, orchestrates the expression of genes linked to inflammation and cell survival. Research by (Subramaniam et al. 2007) underscores silymarin's capacity to impede NF-κB activation, thereby dampening the inflammatory cascade within the organism. These mechanisms contribute to silymarin's inhibition of NF-κB by suppressing NF-κB activation, as silymarin interferes with the signaling pathways that activate NF-κB, preventing its transport to the cell nucleus and from in doing so, it reduces the expression of proinflammatory genes and attenuates the overall inflammatory response (Serce, et al ,2016). Silymarin inhibits the activity of the IKK complex, which plays a crucial role in the phosphorylation and subsequent degradation of the NF-κB inhibitor protein (IκB). By inhibiting the IKK complex, silymarin prevents IκB degradation, resulting in the retention of NF-κB in the cytoplasm and inhibition of transcriptional activity while modulating NF-κB-dependent genes. Silymarin reduces the expression of various NF-κB-dependent genes involved in inflammation, including cytokines, chemokines, adhesion molecules, and inflammation-promoting enzymes. This additional modification contributes to the comprehensive anti-inflammatory effect of silymarin (Teo, et al, 2008).

b. Relieve inflammatory disorders:

By interfering in the complex molecular pathways that fuel inflammation and its action on modulating NF-κB activity, it places it as a promising therapeutic agent in combating inflammatory disorders (Raja, R.) as silymarin provides relief in chronic nonsteroidal inflammatory conditions (Mani et al., 2007) where it has an anti-inflammatory effect. For tissue, muscular, and even bone infections (Muller, et al, 2001). Making it a natural ally in the face of non-steroidal inflammatory attacks such as rheumatoid arthritis, inhibiting silymarin can help (Asrani, et al, 2019).

The activity of NF-κB in reducing joint inflammation and alleviating symptoms associated with rheumatoid arthritis and inflammatory bowel disease (IBD) via the anti-inflammatory properties of silymarin may provide protection against colitis and aid in the management of IBD by attenuating the inflammatory response in the gastrointestinal tract (Wianowska, et al. .2014).

c. Suppression of pro-inflammatory cytokines:

NF-κB regulates the production of many pro-inflammatory cytokines, such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α). Silymarin can suppress the production of these cytokines by inhibiting NF-κB signaling, thereby decreasing the inflammatory response (Mani, et al, 2007).

The mechanism of suppression by silymarin is the inhibition of nuclear factor-κB (NF-κB) signaling, an inducible factor that plays a major role in regulating the production of proinflammatory cytokines (Subramaniam, et al., 2007). Upon activation, NF-κB activates the expression of genes associated with pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α. Silymarin inhibits NF-κB, preventing it from entering the cell nucleus and activating genes that stimulate inflammation. Silymarin's inhibition of NF-κB activity block production of proinflammatory cytokines and thus reduces the inflammatory response (Wianowska, et al. 2014).

This suppressive effect of silymarin is due in part to its antioxidant effect. When cells experience oxidative stress and inflammation, NF-κB is activated. By neutralizing ROS and reducing oxidative stress, silymarin can inhibit NF-κB activation and reduce inflammation (Subramaniam, et al, 2007). There are studies suggesting that silymarin can also inhibit other signaling pathways associated with NF-κB activation, such as the MAPK pathway (mitogen-activated protein kinase pathways), and this contributes to the inhibition of inflammation (Müller et al., 2001).

d. **Making changes in the inflammatory environment:**

Silymarin can also modify the expression and activity of other inflammatory mediators such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). These enzymes participate in the production of prostaglandins and nitric oxide, respectively, which are important mediators of inflammation. By downregulating COX-2 and iNOS expression, silymarin can alleviate the inflammatory process (Wianowska, et al. 2014).

e. Antioxidant activity

Silymarin has powerful antioxidant properties, contributing to its anti-inflammatory effects. Inflammation is often associated with increased oxidative stress, which results in the production of reactive oxygen species (ROS) that exacerbate inflammation. The antioxidant activity of silymarin helps neutralize reactive oxygen species and reduce oxidative stress, thereby alleviating inflammation (Mani et al., 2007).

Significant silymarin gains result in:

1. Antioxidant: Silymarin acts as a powerful antioxidant, helping to protect cells and tissues from damage resulting from blood sugar. It acts by neutralizing ROS (Tupe, et al., 2013).
2. Anti-inflammatory: Silymarin has anti-inflammatory effects, as it works to get rid of organic materials and relieve other symptoms. It works by eliminating inflammation thereby eliminating inflammation (Teo, et al,2008).
3. Blood prevention: But it is also known that silymarin prevents and prevents blood. The antioxidant properties of silymarin can lead to weight loss, control liver inflammation, and improve liver function (Mueller et al. 2001).
4. Against tumors: There is unlimited evidence of silymarin's ability to generate some different types. This property is partly due to its oxidative effect in regulating cancer cells and halting cancer cell proliferation (Serce, et al, 2016).
5. Heart protection: There is some research indicating that silymarin may be limited to protecting the heart from immune deficiency, nutritional damage, and infections. It can be limited to improving heart health but also heart and blood diseases (Asrani, et al, 2019).

5. Effect on infected cells and their elimination:

Silymarin exerts its effect on infected cells through multiple mechanisms, which ultimately leads to their elimination according to several methods in terms of eliminating and removing the cell:

1. Stimulating programmed cell death:

A group of studies have shown that silymarin has the ability to stimulate programmed cell death in various types of damaged cells. This is due to the fact that silymarin activates caspases, which are known as enzymes responsible for initiating and implementing the programmed cell death process (Teo, et al, 2008).

Silymarin helps activate the process of cellular programming for death (programmed cell death) to eliminate a group of cells that have been partially or completely damaged depending on the result of the damage and what is

inflicted on them, that is, they cannot be repaired or have undergone abnormal changes such as cancer cells (Serce, et al, 2016).

The process of programmed cell death (programmed cell death) is a vital mechanism that works regularly to remove damaged, unhealthy cells from the body (Mani, et al, 2007).

This process that we mentioned depends on a series of events that stimulate the cell to activate a group of important proteins (such as caspases) that carry out a group of interactions for the process of cell lysis and breakdown by activating caspases (Asrani, et al, 2019).

The damaged cell population is naturally broken down, catabolized and broken down within the targeted body site and this in turn contributes to the elimination of the damaged and unhealthy mutant cells detected (Taub et al., 2013).

2. Cell cycle arrest:

Silymarin has the complete ability to stop the progression of the cell life cycle at any stage, such as the G1 stage (Asrani, et al, 2019).

Within this stage, the cell cycle is intervened, as silymarin stops any reproduction or spread of damaged cells and ultimately removes them (Teo, et al., 2008).

The cell life cycle is a set of sequential events according to common mechanisms linked to what happens within the cell and related to its growth, preparation for reproduction, actual reproduction, and division. The cell cycle consists of several phases, including G1 phase, S phase (in which DNA is copied), G2 phase, and finally mitotic phase (M phase) (Müller et al., 2001).

Research indicates that silymarin can interfere with several stages of the cell cycle, especially in the G1 phase (Serce, et al., 2016). Silymarin inhibits the activity of some important proteins associated with the regulation of the cell cycle, which leads to stopping the progress of cells in the cell cycle and preventing them from multiplying and spreading, by interfering with the cell cycle. Silymarin also decreases cellular growth and proliferation of damaged cells (Mani et al., 2007). This contributes to the elimination of damaged cells and preventing their spread to other areas of the body (Serce et al, 2016). Cell cycle arrest is a process that prevents cells from progressing through normal phases of their biological cycle. Silymarin acts by:

1. Mechanism of inhibition of cell cycle control proteins: Silymarin has the ability to inhibit the activity of actual cell cycle control proteins such as cyclin-dependent kinase (CDK) and cyclins. These proteins play a major role in the process of regulating cell growth during the phases of the cell cycle. This is done by inhibiting the activity of these proteins, and therefore silymarin can stop cell growth at certain stages of the cell cycle (Wianowska, et al. 2014).
2. It works according to a mechanism to inhibit gene expression: Silymarin also inhibits the expression of some genes related to cell cycle regulation, as it carries out an actual process of inhibition by controlling and stopping the biological processes that cause the disease. cell to progress through the phases of the cell cycle (Müller, et al., 2001).
3. Working to activate cell arrest signaling pathways: Silymarin can activate signaling pathways within the cell structure that lead to cell cycle arrest. For example, silymarin activates p53, one of the most important activators for cell arrest and repair of genetic damage (Asrani, et al., 2019).

Inactivation of cell survival pathways:

Silymarin reduces survival signals that support the growth and reproduction of damaged cells and thus will help in eliminating them (Vo, et al, 2017).

The way these pathways are inhibited is through a complex process, whereby silymarin interferes with cell survival pathways such as the PI3K/Akt pathway, which are typically disrupted in many diseases, including cancer. (Taub et al., 2013)

This active activity of Akt will activate many intracellular processes that are important for survival and growth, such as increased energy generation, cell proliferation, and inhibition of apoptosis. There is a lot of research indicating that silymarin can directly or indirectly inhibit the PI3K/Akt pathway (Mani et al., 2007).

Inhibition of this pathway indicates the presence of silymarin. It reduces the activity of the Akt protein. The PI3K/Akt pathway is also one of the important pathways in controlling cellular growth and survival, as the PI3K protein stimulates the production of an intracellular signal known as PIP3 (Tupe, et al, 2013).). Which in turn activates Akt (Mani, et al, 2007).

Other related factors are important because they help reduce the survival signals that support the growth and proliferation of damaged cells (Vo, et al., 2017). Therefore, this intervention in cell survival pathways could be of great importance in the treatment and prevention of diseases associated with cell interactions. and defects such as cancer, inflammatory diseases, and immunological diseases (Mani et al. 2007).

Antiangiogenic effects:

One of the important properties of silymarin is its ability to restrict blood flow to these cells. Silymarin hinders their ability to obtain nutrients and oxygen, ultimately killing them (Malekzadeh, et al., 2013).

The process of creating new blood vessels is known as angiogenesis, or vascular perfusion, and is a vital process necessary for cancer cells to grow and supply nutrients and oxygen. By blocking angiogenesis, silymarin limits the availability of resources to cancer cells, inhibiting their growth and spread and contributing to their killing (Vo, et al, 2017).

This means that it inhibits the formation of new blood vessels that support the growth and spread of damaged cells, especially in tumors. This anti-angiogenic property may be of great importance in the field of cancer treatment, where silymarin could be used as a natural agent. A compound that prevents the growth of blood vessels associated with the tumor, thus reducing the expansion of the tumor and preventing its spread to other areas of the tumor. body. (Malikzadeh, et al., 2013).

1. **Silymarin works as an antioxidant:**

which means that it contributes to reducing the harmful effects of free radicals and reduces oxidative stress within cells (Soysal,2009).. Free radicals are unstable molecules that form in the body as a result of natural metabolic processes and external factors such as pollution, smoking, and radiation. If these free radicals accumulate in large quantities (Malekzadeh, et al,2013).

They can cause oxidative damage to cells and tissues, as excess oxidative stress and oxidative damage to cells are contributing factors to many chronic diseases such as heart disease, cancer, and liver disease. Through its ability to eliminate free radicals and reduce oxidative stress, silymarin protects cells from oxidative damage caused by these harmful factors (Tupe, et al,2013).,.

Silymarin also promotes the removal of cells that suffer from irreparable damage. When cells are exposed to severe damage and are no longer repairable, silymarin works to enhance the process of removing them from the body, which maintains the health and safety of tissues and reduces the chances of developing diseases (Soysal,2009).

2. **Antidiabetic activity of silymarin:**

Silymarin has demonstrated promising antidiabetic properties in various studies. It has been observed to reduce fasting blood sugar levels and normalize insulin levels, making it beneficial for diabetic individuals (Soysal,2009).

Experimental animal models of diabetes have shown effective hypoglycemic and hypoglycemic activities of silymarin (Radek, et al., 2007), It improves glucose metabolism by enhancing insulin sensitivity and enhancing glucose uptake into peripheral tissues such as skeletal muscle and adipose tissue. Which results in lower blood sugar levels during fasting (Akhtar et al ,2015)

Silymarin exerts its effects by enhancing insulin secretion from pancreatic beta cells or by improving target tissue response to insulin. By regulating insulin levels, it helps in maintaining glucose balance in the body (Tupe, et al,2013)

Additionally, silymarin acts as a hypoglycemic agent by inhibiting enzymes involved in carbohydrate metabolism, such as alpha-amylase and alpha-glucosidase (Radek, et al., 2007),

By inhibiting these enzymes, silymarin slows the breakdown and absorption of carbohydrates in the intestine, which results in lower postprandial (after-meal) blood glucose levels (Akhtar et al ,2015).

3. Hypocholesterolemia activity of silymarin:

The effects of silymarin and its polyphenolic part, according to a group of studies that dealt with the subject, showed that the group of mice fed a high-cholesterol diet showed that silymarin reduces cholesterol levels in the liver and plasma of mice (Tupe, et al., 2013).

The reason for this is that hypocholesterolemia activity triggers several mechanisms that are supported by experimental evidence (Krystyjan et al., 2022). These mechanisms mediate :

First: The mechanism of HMG-CoA reductase inhibition: It is clear that silybin works to reduce the activity of HMG-CoA reductase in vitro (Suray, 2023).

This enzyme functions in the joint process of cholesterol synthesis in the liver by inhibiting HMG-CoA reductase. This will cause silymarin to work specifically in reducing cholesterol production, resulting in lower cholesterol levels (Magrani, et al, 2004).

Enhancement of LDL Binding: Silymarin has been shown to have the ability to enhance the binding of low-density lipoproteins (LDL) to rat liver cells. (Maaloul, 2024).

This may increase the liver's uptake of LDL and thus reduce levels of LDL cholesterol in the circulation (Zhang, et al, 2018).

Reduced liver cholesterol content: Silymarin supplements reduce the liver cholesterol content in rabbits fed a high-cholesterol diet (Tupe, et al, 2013).,. By reducing the accumulation of cholesterol in the kidneys. From this, we conclude that silymarin plays a role in maintaining cholesterol homeostasis (Zhu, et al, 2017).

Reducing Plasma Cholesterol and LDL Cholesterol Levels: Silymarin has been shown to reduce plasma cholesterol levels and LDL cholesterol levels in hyperlipidemia rats (Magrani, et al, 2004). Thus, this effect is beneficial in preventing the development of atherosclerosis and other cardiovascular complications associated with high blood cholesterol levels (Zhu, et al., 2017).

Reduced Cholesterol Absorption: Silymarin and its polyphenolic charge significantly reduced cholesterol absorption in mice fed a high-cholesterol diet (Maghran, et al, 2004) and thus this reduction in cholesterol absorption contributes to the overall decrease in cholesterol levels observed in the liver. and plasma (Fu et al., 2016).

There are many mechanisms that plants use to produce benefits in the body, and these mechanisms include many different processes and interactions. Among these mechanisms:

- Effect of active compounds: This plant contains within its composition a variety of active compounds that can positively affect human health, such as vitamins, minerals, amino acids, flavonoids, polyphenols, terpenoids, carotenoids, and others. These compounds interact with many vital processes in the body. The body, such as metabolism, immunity, metabolism, etc. (Farghaly, et al., 2015)
- Effect on the immune system: Plants can affect the human immune system, either by enhancing or regulating it. Some plants contain compounds that enhance the immune system's response, while others contain compounds that reduce body inflammation and strengthen the immune response.(Duan, 2005)
- Effect on metabolism and metabolism: Plants can affect metabolism and metabolic processes in the body, which leads to improving the health of various organs and systems. For example, some plants help regulate blood sugar levels, promote digestion, and improve gastrointestinal function(Maaloul,2024).
- Effect on the nervous system: Some active compounds in plants can affect the functions of the nervous system, which contributes to relieving stress, improving mood, and promoting good sleep.(Surai,2023)

These mechanisms interact with the body in several ways, including absorption through the digestive tract, absorption through the skin, response through the nervous system, interaction with enzymes in the body, and others. These compounds interact with many organs and systems in the body to achieve desired health benefits.

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