A Review On Pharmacological Properties Of Silybum Marianum

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Abstract- *Silymarin is the active ingredient in Silybum marianum (milk thistle), a flavonolignan with C-25. Milk thistle has many traditional values. It is used as a vegetable, as a salad, as a bitter tonic and as a galactagogue in nursing mothers and for various ailments such as liver complications, depression, indigestion, congestion of the spleen, varicose veins, diabetes, etc. Amenorrhea, uterine bleeding and menstrual cramps. This chapter attempts to comprehensively discuss the potential of silymarin in the treatment of chronic diseases. Information was provided on the modulation of cell signalling by silymarin and its effects on various diseases such as liver diseases, inflammatory diseases, cancer, neurological disorders, skin diseases and hypercholesterolemia.*

Keywords- Antioxidant, Cancer, Liver, Medicinal plant, Silymarin

I. INTRODUCTION

Silybum marianum L. (Milk thistle) belongs to the Carduus marianum family and is an ancient medicinal plant that has been used for centuries to treat various diseases such as liver and gallbladder diseases, as well as to protect the liver from snake bites and insect bites. , mushroom poisoning and alcohol abuse (1). This plant is found in Kashmir, North America, Canada and Mexico. It has large leaves and spiky red-purple flowers and the medicinal part of the plant consists of seeds or fruits (2).

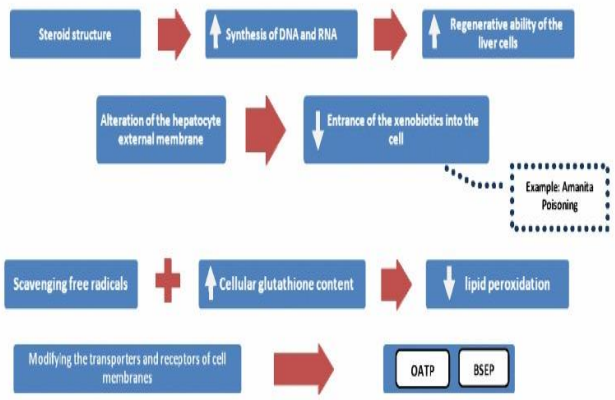
Milk thistle was first cultivated in Europe and used as a liver tonic because it was said to dissolve congestion in the liver and spleen and was therefore effective against jaundice (Nicolas Culpepper, 1616-1654)(3). Additionally, this herb has been used for centuries as a natural remedy for upper gastrointestinal and digestive problems, liver and biliary tract diseases, menstrual disorders, and varicose veins.However, the first use of milk thistle was for its hepatoprotective and antioxidant effects. The active ingredient of this plant is silymarin, a complex of other ingredients, mainly silybin A, silybin B, isosilybin A, isosilybin B, as well as other flavonolignans such as silycristin, neosiliermin, silyermin and silydianin, which are contained in its fruits. and seeds. compared to the other parts.

Silymarin has also been shown to work on various diseases of various organs such as the prostate, lungs, central nervous system, kidneys, pancreas and skin (9). Silymarin also has , immunomodulatory and anti-inflammatory properties, as well as antioxidant properties, scavenges free radicals and increases glutathione concentration, so it can be used in the treatment of hepatitis, liver cirrhosis and fungal poisoning (5, 7, ten). According to pharmacological studies, Silymarin is considered a safe herbal product because the use of physiological doses of Silymarin is not toxic unless therapeutic doses are administered incorrectly (10-12). The main reported side effects include headache, gastroenteritis and dermatological symptoms, the most common of which are gastrointestinal symptoms (1). Milk thistle extract is currently sold in capsules and tablets containing Silymarin and villain with increased bioavailability under trade names such as Liverpool, Suicide and Legal on (6). In animal models, the active ingredients of Silymarin showed a protective effect against hematologic drugs used in chemotherapy against tuberculosis (13). The antioxidant properties of Silymarin have been reported to increase superoxide dismutase activity in erythrocytes and lymphocytes (3). Silymarin can also calm the hepatocyte membrane and prevent xenobiotics from entering the cell via the intrahepatic circulation. Silymarin can readily bind to iron and inhibit the reduction of glutathione in human hepatocytes (3). Silymarin is able to modulate the immune system and increases the secretion of IFN, IL-4 and IL-10 in cultures with lymphocytes. Its antitumor effect is associated with factors and growth inhibition, induction of endothelial cell apoptosis via the p53-dependent pathway involving Bcl-2/BAX, release of cytochrome c, Apaf-1, and activation of caspase-3 and PARP (3). , 14).

Mechanism of Action:-

The different mechanisms of action of Silymarin are as follows: increasing the regenerative ability of liver cells by increasing DNA and RNA synthesis, Silymarin being a steroid structure; Change in the structure of the outer membrane of hepatocytes, which prevents the entry of xenobiotics into the cell (a notable example of such a mechanism is poisoning by Manila mushrooms); It scavenges free radicals and increases cellular glutathione content, leading to inhibition of lipid

peroxidation ; Another mechanism of action of Silymarin is the modification of cell membrane transporters and receptors, such as: B. ABC transporters (PGP), organic anion transport peptides (OATH), the salt export pump of the bile duct and transporters.



Cancer prevention and treatment Effect of Silymarin or Bilibili on breast cancer (27-28), ovarian cancer, lung cancer (29), skin cancer (30), prostate cancer (31-33), cervical cancer, breast cancer, bladder cancer, liver cancer (34) and colon cancer (35) (6). The mechanism of action of villain is related to the antioxidant and radical scavenging activity as well as the specific interaction with receptors and the modulation of various cell signalling pathways, for example NF-kappa B, suppression of signalling EARMARK/ERK1/2 and IGF- Receptor signalling (9). Furthermore, the effect of Silymarin on UV radiation was demonstrated by increasing the expression of tumour suppressor genes p53 and p21CIP1 (4,36). Silymarin has been proven to have properties in various types of cancer, which is one of the most important methods of cancer treatment. In addition, previous studies have demonstrated the effects of Silymarin and villain in human umbilical vein endothelial cells (HAVE) in a dose-dependent manner through the mechanism of reducing vascular endothelial growth factor (VEGA) and metalloproteinase-2 secretion. The matrix (MMP). -2) (1, 6). Negative regulation of EGFR signalling by Silymarin and Bilibili occurs through various mechanisms, such as: B. Inhibition of the expression and secretion of growth factors, prevention of growth factor binding and activation of EGFR, as well as the destruction of mitogenic processes that are responsible for antitumor activity in tumour cells (37). This inhibition of mitogenic signalling pathways in prostate cancer results in impairment of cell cycle regulators, growth inhibition and androgen-independent loss of prostate cancer cells and expression of protein-binding protein, a growth factor similar to insulin 3 (1). However, numerous in vitro and in vivo experiments on tumour models have shown no significant differences in biological activity between Silymarin and villain (11). is formed through lipid peroxidation and leads to the formation of MDA-DNA adducts that cause frameshift mutations as a link between oxidative stress and human cancer (38). Silymarin treatment significantly reduces the production of MDA-DNA adducts and serum markers of hepatocellular carcinoma, such as alpha-fetoprotein, antigen, amino transferase, alkaline phosphatase, lactate dehydrogenase nucleosidase.

Multidrug resistance is a major problem in the effective treatment of cancer, which is related to the overexpression of P-glycoprotein (PGP) or multidrug resistance-related protein 1 (MRP1). Silymarin increases the absorption and bioavailability of chemo pharmaceuticals such as daunomycin, and in tumour cells by inhibiting P-glycoprotein (PGP), an MRP1-mediated drug transporter, and breast cancer resistance protein (BRCP). (4, 6, 9). Silymarin can be used in combination therapy with other chemotherapy drugs, while villain is primarily useful as a substance that protects the liver from oxidative stress caused by chemotherapy drugs. The growth inhibitory effects and apoptotic efficacy of villain have also been demonstrated in cultured prostate cancer cells and rat cancer cells (33). Furthermore, Silymarin inhibits the growth of ?-catering, which inhibits the proliferation of HepG2 hepatocellular carcinoma cells.?-Catering is an important factor in the cell adhesion complex. It stimulates T-cell transcription factor and plays an important role in regulating the oncogenic process as well as anti-apoptotic effect in various tumours. On the other hand, the mitochondrial membrane potential of HepG2 cells decreases under the influence of Silymarin, leading to disruption of membrane permeability, thereby transferring cytochrome c from the intermembrane space to the cytoplasm (11). While apoptosis is induced by p53 through the activation of pro-apoptotic genes, p53 levels are increased in a dose-dependent manner by Silymarin treatment, leading to the release of cytochrome c and activating many pro-apoptotic genes. 1 and caspase-9. Silymarin has therefore been shown to have growth inhibitory effects by inhibiting cell proliferation and inducing apoptosis (11).

Kidney protection:-

The effects of Silymarin were studied in rats in models of Allan-induced diabetes. Allan produces reactive oxygen species (H2O2, O2, and ?OH) (39), which damage kidney tissue (40-41). Silymarin was administered 20 days after 9 weeks of Allan treatment and was effective in treating kidney tissue damage. It has an antioxidant effect by increasing the genetic expression of antioxidant enzymes and a number of important protective mechanisms against the harmful effects of free radicals, including superoxide dismutase, glutathione peroxidase and catalase. Therefore,

Silymarin can be used as a drug to treat diabetic nephropathy (42). Oxidative stress (ROS) reduces glomerular filtration. Treatment with Silymarin or vitamin E improved the change in serum creatinine concentration in dogs treated with gentamicin (43). In another study, Silymarin was able to counteract the renal toxicity caused by cisplatin and isocyanide without reducing the antitumor efficacy of these drugs (6, 44-45). Ferrous (Feint) causes nephrotoxicity and kidney cancer by inducing redox-active iron species, reactive oxygen species, and lipid peroxidation (LPO), which can damage cell membranes and molecules such as DNA. The formation of 8-hydroxyguanosine leads to mutations in DNA (46). Silymarin has an adjuvant effect on Fe-TNA-induced LPO. This protection may be related to its antioxidant and anti-free radical effects. NFL (nuclear factor kappa B) activates many oncogenic processes, e.g. B. cellular inflammation, proliferation, inhibition of apoptosis by increasing the expression of other genes (nitric oxide synthase, 2 and proinflammatory cytokines, e.g. tumour necrosis factor alpha (TNF)-?). And interleukin-6. Therefore, suppression of NFL is considered a useful plan to control carcinogenic effects. NFL activation can be suppressed by Silymarin due to some stimulants such as formal esters, mosaic acid and ceramic. These results suggest that Silymarin could be a strategy for treating kidney cancer by reducing certain tumour-inducing factors in animal models. (46). In a human study, administration of Silymarin (210 mg/day) for 8 weeks to patients undergoing peritoneal dialysis inhibited the action of inflammatory, particularly TNF- (47). The inhibitory effect of TNF on erythropoiesis and bone marrow suppression by preventing the production of Synthroid colony forming units (E-CFU), a precursor of red blood cells during early development, leads to problems with haematological status in patients with advanced renal failure. In this study, 40% of patients had a significant response and haemoglobin levels increased after 8 weeks of Silymarin administration. Therefore, it can be assumed that Silymarin could be used to treat inflammatory anaemia in patients on peritoneal dialysis (47).

Neural effect:-

High oxygen utilization, enormous amounts of polyunsaturated fatty acids, high levels of free iron ions, and low antioxidant protection make brain tissue susceptible to damage from reactive oxygen species (48). Silymarin administered at a dose of 200 mg/kg/day significantly reduced protein oxidation in the hippocampus and cortex of aged rats compared to young rats. Silymarin can be used as the drug of choice against Alzheimer's disease, in which protein oxidation is an important early event. According to previous studies, Silymarin has antioxidant effects on the central nervous system, which allows it to enter the central nervous system across the blood-brain barrier (BBB)(48-51). Administration of 200 mg/kg Silymarin also reduced 6-hydroxydopamine (6-OHDA)-induced turning behaviour in rats, and neurons in the substantia nigra pars compact were protected from its toxicity, suggesting a dose-dependent neuroprotective effect of Silymarin suggests 6.-ODHA toxicity, reduction of oxidative stress and via the estrogenic pathway (52). It is also known that Silymarín can increase the concentration of certain neurotransmitters in the brain. Aqueous and ethanol extracts of Silymarín were used in the modified forced swimming test study on mice. The results showed that the ethanol extract had no effect on the immobility time of mice, while the aqueous extract significantly reduced it, leading to the conclusion that aqueous Silymarín extract has antidepressant effects in animal models (53).

Immunomodulator:-

Based on flow cytometric analysis of splenocytes, Silymarín was found to significantly reduce the number of CD3+ T cells and the CD4+ population at a dose of 10 mg/kg. In this study, mice were exposed to different doses of Silymarín (0, 10, 50, or 250 mg/kg, intraperitoneally, once daily for 5 days). A phytohemagglutinin-induced increase in T cell proliferation was observed in the group treated with the lowest dose. Doses of 10 and 50 mg/kg Silymarín increased LPSinduced B cell baryogenesis and reduced IL-2 and IL-4 expression. However, the mRNA expression of TNF, INS, IL-1 and IL-6 increased in a dose-dependent manner. Consequently, in vivo exposure to low doses of Silymarín inhibits T cell function and, at higher doses, stimulates inflammatory pathways (4). In other studies, Silymarín significantly reduced IL-2 and gamma interferon (IFN) production and blocked nuclear translocation of transcription factor lb (NFL), which activates IL-2 transcription. It can be concluded that Silymarín inhibits T cell activation and proliferation, particularly by affecting NFL activation or translocation pathways (54).

Protective effect against environmental toxins:-

In a study in healthy volunteers, Silymarín was shown to prevent the cytotoxic effects of Benz(a)parent on peripheral blood cells by stabilizing cell membranes, increasing the GSH/GSSG ratio, restoring enzymes that metabolize glutathione, and Active ingredients eliminated from lipids. Peroxidation, protein oxidation, and functional stimulation of antioxidant enzymes such as catalase and superoxide dismutase (60).

Toxicology and side effects:-

The tolerability of silymarin is good and only mild gastrointestinal disorders and mild allergic reactions, urticaria, nausea, headache, arthralgia, itching and mild laxative symptoms have been reported. In animal studies, silymarin has been shown to be non-toxic and symptom-free at maximum oral doses of 2,500 and 5,000 mg/kg. Silymarin has also been shown to be nonteratogenic and has no postmortem toxicity (2, 5, 33). Since no significant toxicity of silymarin has been found in human studies, this substance can be used as a dietary supplement together with anti-tuberculosis drugs (13). Although silymarin is safe, little is known about its mechanism of action and drug-food interactions (3).

II. CONCLUSION

Silymarin has a wide range of in vitro and in vivo mechanisms, such as: the modification of cell transporters, antioxidant, anti-inflammatory, anti-apoptotic and dose-dependent mechanisms. It can therefore be used as a promising drug in complementary medicine.

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