The Protective Effect of Milk Thistle Against Drug-Induced Renal Illnesses: A Review

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ABSTRACT:

Introduction: Nephrotoxicity is one of the most frequent kidney problems and happens when the body becomes exposed to medicine or toxin. Because renal tubular cells have metabolic activities, nephrotoxin can produce toxic components and cause damage. Paracetamol drug is safe when taken in therapeutic doses as an antipyretic and analgesic agent but its excessive doses may result in life-threatening renal impairment due to the generation of reactive-toxic metabolites. Scientific efforts are concentrated on discovering preventative or therapeutic medications to shield against the toxicity brought on by paracetamol due to nephrotoxicity. Silymarin, a medicine, is extracted from polyphenolic compounds found in the milk thistle plant. This plant has antioxidant, anti-inflammatory, anti-cancerous, and other properties and is the most commonly used drug for hepatic illnesses. Also, it has renal-protecting effects. **Objective:** This review research highlights the nephroprotective of silymarin against paracetamol-induced renal damage.

Key words: Kidney, Milk thistle plant, Nephroprotective, Paracetamol, Silymarin.

التأثير الوقائي لحليب الشوك ضد امراض الكلى التي يسببها الدواء: مقال مراجعة

الخلاصة

المقدمة: تعتبر السمية الكلوية من أكثر مشاكل الكلى شيوعًا وتحدث عندما يتعرض الجسم للأدوية أو السموم. نظرًا لأن الخلايا الأنبوبية الكلوية لها أنشطة استقلابية ، يمكن أن تنتج السموم الكلوية مكونات سامة وتسبب الضرر. يعتبر عقار الباراسيتامول آمنًا عند تناوله بجرعات علاجية كعامل خافض للحرارة ومسكن ، لكن جرعاته الزائدة قد تؤدي إلى اختلال كلوي يهدد الحياة بسبب إنتاج المستقلبات السامة التفاعلية. تتركز الجهود العلمية على اكتشاف الأدوية الوقائية أو العلاجية للوقاية من السمية التي يسببها الباراسيتامول. من ناحية اخرى, يعتبر سيليمارين دواء يُستخرج من مركبات البوليفينول الموجودة في نبات شوك الحليب. يحتوي هذا النبات على خصائص مضادة للأكسدة ومضادة للالتهابات ومضادة للسرطان وخواص أخرى وهو أكثر الأدوية شيوعًا لعلاج أمراض الكبد. كذلك هذه المادة ، لها تأثيرات حماية للكلى . **الهدف:** يسلط بحث المراجعة هذا الضوء على الحماية الكلوية للسيليمارين ضد التلف الكلوي الناجم عن الباراسيتامول.

الكلمات المفتاحية: الكلية، باراسيتامول، سيليمارين، نبات حليب الشوك، واقي-كلوي.

INTRODUCTION:

The kidney is a delicate and dynamic organ in charge of maintaining homeostasis and controlling the extracellular space (1). It is essential for maintaining the body's physiological functions, including hormone synthesis and secretion, plasma osmolarity maintenance, acid-base equilibrium, and water and

electrolyte homeostasis. Since the kidneys are the primary organs through which medications are eliminated, prior data suggested that the deleterious effects of both pharmaceuticals and other environmental pollutants could cause changes in how the kidneys operate (2). One of the most frequent causes of acute kidney damage is drug-induced nephrotoxicity. A sudden drop in the glomerular filtration rate (GFR) is referred to as acute kidney injury (AKI), sometimes known as acute renal failure (3). One sign of nephrotoxicity is an alteration in renal function as evaluated by the GFR, blood urea nitrogen (BUN), serum creatinine (SCr), or urinary output (4).

One of the most extensively used and well-liked medications for the treatment of pain and fever is paracetamol. Although paracetamol is thought to be a safe medication, an overdose might trigger serious liver and kidney damage and even fatality. The main organs involved in the metabolism of paracetamol are the liver and, to a smaller degree, the kidneys and gut (5). The hepatic cytochrome P450 (CYP450) oxidative system produces the reactive intermediate n-acetyl-p-benzoquinone imine (NAPQI), which is linked to paracetamol toxicity. NAPQI binds to cellular components in excess and can destroy hepatocytes when its synthesis surpasses the body's ability to eliminate it, as can happen in overdose (6). When NAPQI is not detoxified, lipid peroxidation (LPO) starts, which leads to kidney damage. It was stated that free radicals generated by exposure to drug toxicity and oxidative damage in an organism perform a significant role in paracetamol-related hepato-renal damages (5). There is currently no known antidote for paracetamol-induced renal damage (7).

Medical plants may work as a crucial source of possibly useful novel compounds for the development of effective therapy to combat a diversity of kidney ailments (8). An interesting example is the milk thistle plant. This plant has a long history of use in traditional medicine as a remedy for diseases like liver diseases, renal issues, fever, cardiac disorders, gastronomic disturbances, and others (9). Silymarin is an active extract from the seeds of milk thistle that has exerted potent hepatoprotective effects (10).

Data on silymarin's renal effects are less well-known than those on its hepatic effects. Studies assessing the hepatic effects of silymarin have provided information on its impact on renal functioning (10). Silymarin was found to protect against diabetic nephropathy and drug and chemical-induced nephrotoxicity (11). In vitro and in vivo studies were shown the silymarin's capacity to reduce oxidative stress injuries from paracetamol, aflatoxin B1, carbon tetrachloride, cisplatin, and doxorubicin. This benefit might result from reducing the danger of oxidative stress damage and raising the kidney's thiol level (12).

This review article is focused on the summarization of the pathophysiology of paracetamol-induced nephrotoxicity and an overview of the milk thistle plant, in addition to specific reports about the nephroprotective effect of silymarin in some animals' experimental studies.

Pathophysiology of Paracetamol Toxicity

It is recognized that paracetamol toxicity largely affects hepatic as well as extra-hepatic tissues (13). Its main toxicity is related to drug metabolism in these tissues (14). When paracetamol is consumed at the recommended therapeutic dose, most paracetamol undergoes a phase II conjugation reaction in hepatocytes to form glucuronide and sulfate conjugates which are excreted in the urine. Only a small amount of paracetamol was excreted unchanged in the urine. A very small amount (approximately

5-9%), undergoes a phase I metabolic reaction by CYP450 (especially CYP 2E1) which oxidize paracetamol into a highly reactive metabolite, NAPQI (15). Typically, NAPQI is rapidly detoxified by conjugation with hepatic reduced glutathione (GSH) and eliminated by the kidneys (16). However, in paracetamol overdose, this mechanism becomes saturated and exceeds the capacity to detoxify NAPQI. Excess NAPQI causes oxidative stress-related toxicity. Increased levels of NAPQI oxidize tissue macromolecules such as lipid or protein-thiols and alter the homeostasis of calcium after depleting GSH which has led to oxidative damage and thus enhances cellular injury and organ dysfunction including renal damage (2).

Nephrotoxicity owing to paracetamol high dose is found to be relatively less frequent than hepatotoxicity. Acute renal failure after an overdose of paracetamol can occasionally happen as a secondary effect of hepatotoxicity (17). However, even in the absence of liver damage, acute renal failure can still develop (18). Paracetamol-induced renal insufficiency affects 1-2% of individuals (17,19).

There is debate concerning how paracetamol damages the kidneys (20). Probable causes originate from the microsomal CYP-450 systems' local generation of arylating intermediate, albeit to a smaller level than do hepatocytes. The discovery of paracetamol protein adducts in kidneys has established that paracetamol is oxidized to NAPQI. The proximal tubules of the renal cortex, in particular, are where the CYP-450 systems are most active. Consequently, paracetamol renal toxicity is likely limited to this region of the kidneys (17). Other mechanisms involve the de-acetylation of paracetamol to p-aminophenol in the renal cortex, a molecule that is selectively nephrotoxic and induces necrosis at the renal cortex. P-aminophenol formed in therapeutic doses is conjugated with glutathione and excreted inactive glutathione conjugate. In chronic or high paracetamol doses and with depletion of GSH, p-aminophenol binds to renal biomolecules by covalent bonds, causing renal damage. Paracetamol even has harmful effects on the renal medulla through inhibition of prostaglandin synthase (19). Paracetamol has been demonstrated to cause apoptosis in murine proximal tubular cells, and endoplasmic reticulum stress is likely to amplify this effect. Another research found that acetaminophen elevates reactive oxygen radicals, including nitric oxide, and that this also leads to cell damage (21). The raised serum urea and SCr levels and decrease in GFR are signs of acute tubular necrosis induced by paracetamol (5,8)

Overview of Milk Thistle Plant

Botanical Aspect

Silybum marianum (*L*.) *Gaertn* sometimes referred to as milk thistle, is a spiny herb belonging to the *Asteraceae* family and is a medicinal herb with a 2,000-year history of usage (22,23). It is an annual or biennial plant, which is native to the Mediterranean region and is currently grown and farmed worldwide (23,24). The ideal growth conditions for milk thistle are high temperatures and dry, rocky soil. It may reach heights of three to ten feet and has an upright stem that bears big, alternate leaves with thorny edges (22,24). It blooms from July to August, with big, reddish-purple flowers on each stem that are followed by a spine (Figure 1). The plant's common name, milk thistle, derives from the milky-white lines that span its leaves (24,25). It is unclear whether milk thistle produces fruits or seeds. According to botany, this plant contains cypselae, which look to be seeded but are

fruits that are shiny brown or grey having spots (24).

The plant's medicinal part is its seeds, and silymarin, a mixture of flavonolignans, is its active component (26). Depending on the stage of floral development, flavonolignan accumulation in seeds is greatest during late blooming (25). However, the whole plant is also employed medicinally to treat disorders of the liver, gallbladder, spleen, and kidney (27).

Figure 1: Milk thistle plant (28).

Chemical Composition

A well-known milk thistle seed dry extract called silymarin includes primarily flavonolignan isomers (about 70%–80%), with the remaining 20–30% unknown but potentially bioactive polyphenolic component (29,30). There are four major flavonolignan isomers in silymarin: silibinin, isosilibinin, silichristin, and silidianin, with silibinin (also called silybin) being the most abundant and physiologically active of these (23,31). The milk thistle extract also contains other flavonoids (such as quercetin, taxifolin, eriodictyol, and chrysoeriol), 15–30% lipids in the form of triglycerides (linoleic 60%, oleic 30%, and 9% palmitic acid), around 30% proteins, sugars (arabinose, rhamnose, xylose, and glucose), tocopherol, sterols with cholesterol, campesterol, and stigmasterol (24,25,32).

Silymarin Bioavailability and Toxicity

The majority of commonly used silymarin commercial products contain concentrated standardized extracts that are 70–80% silymarin despite silymarin's low water solubility (33). Silymarin has a reduced bioavailability as a result of its lipophilic nature and therefore restricted solubility. In an effort to boost silymarin solubility, several commercially approved silymarin formulations, such as tablets, syrups, and capsules, have been manufactured (34). The half-life of silibinin in the plasma is approximately 6 hours, and the blood concentration reaches its peak in 2-4 hours. After gastrointestinal absorption, Silymarin/ silibinin suffers hepatic metabolism, including phases I and II (35). As silymarin is circulated through the enterohepatic system, hepatic cells contain higher quantities of silymarin than serum (35). When administered as a single dose, silibinin reaches its highest levels in the bile within 2–9 hours, and the kidneys remove 1-2% of the dose over a day. However, silibinin

endures considerable biliary excretion (28,35).

Studies on silymarin's overall toxicity have shown that it is fairly low and well tolerated. According to studies, the oral 50% lethal dose (LD50) for rats and the highest tolerated dose for dogs are around 10 g/kg body weight (BW) and 300 mg/kg BW, respectively (29,36). Toxicological studies in rodents established the safety of silymarin to treat liver diseases devoid of toxic effects. Silymarin has rare side effects that may include skin allergic reactions or gastrointestinal distress such as nausea, vomiting, and diarrhea (37).

Beneficial Effects of Silymarin

The major site of action of silymarin in Mammalia is the liver (28). Silymarin has shown the capacity to improve liver function tests by lowering the elevated liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) (38). Silymarin hinders or delays the entry of toxins into the liver cells. As a result, the toxins are eliminated through the kidneys before they can harm the liver. The most dramatic example of this is silymarin's capacity to inhibit toxins from the death cap (fungus *Amanita phalloides*). The *Amanita phalloides* is one of the most famous liver poisons known to people. Silymarin acts relatively similarly to detoxifying alcohol, paracetamol, and some heavy metals (39).

Silymarin's hepatoprotective properties can be explained by its antioxidant properties, which are due to the phenolic character of its flavonolignans (40). Due to its phenolic chemistry, it can donate electrons to stabilize ROS and free radicals (41). These implications may be caused by silymarin's capacity to directly scavenge free radicals created during hepatic APAP metabolism, inhibit free radical formation, maintain the mitochondria's electron-transport chain integrity under stress situations, and promote optimal redox homeostasis of the cell by activating a variety of antioxidant enzymes and non-enzymatic antioxidants, raising cellular glutathione level, and inhibiting LPO (28,42,43). In addition, silymarin increases protein synthesis by boosting RNA polymerase I activity in hepatic cells (28). Moreover, silymarin is thought to have anti-inflammatory, anti-fibrotic, anti-apoptotic, anti-diabetic, anti-microbial, and anti-cancerous effects (9,28) (Figure 2).

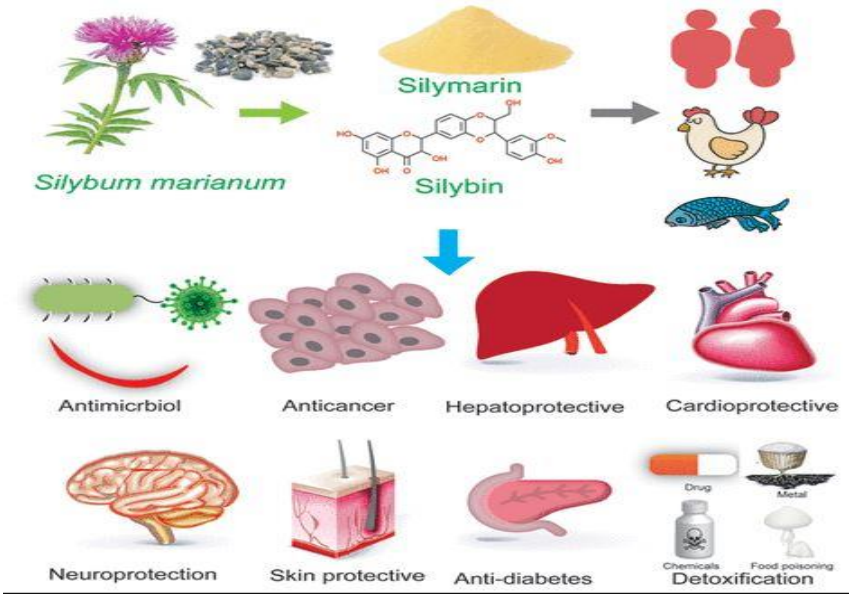

Figure 2: *Silybum marianum's* positive effects on health (44).

Silymarin has also been effective in treating renal conditions. Animal studies have shown its usefulness in an experimental model of renal illnesses (45). Silymarin's renoprotective benefits have mostly been attributed to its anti-oxidant activities and free radical scavenging abilities. In addition to its antioxidant properties, silymarin also possesses anti-inflammatory and cytoprotective effects by inhibiting tumor necrosis factor-alpha (TNF-α) and kinases (46,47). Silymarin increases the expression of the Bcl2 protein, decreases the expression of the Bax protein, and inhibits the cleavage of caspase 3 in kidney tissue, which reduces renal apoptosis and ultimately results in cytoprotection (47,48). Additionally, other associated mechanisms of silymarin's renoprotective actions are its capacity to concentrate in kidney cells and support cell regeneration by enhancing the synthesis of protein and nucleic acids (33), metal chelation, repair and removal of damaged molecules, and/or mitochondrial protection (48), as well as prevention of neutrophil migration and production of leukotriene and prostaglandin, are additional interrelated mechanisms of silymarin's renoprotective effects (49).

Silymarin's hepato-renal protecting effects are due, at least in part, to its capacity to regulate tissue oxidant and antioxidant state, action as a free radical scavenger and LPO inhibitor, and stimulation of endogenous antioxidant processes. Additionally, it stimulates RNA and protein formation, which is critical for renal and hepatic repair processes (4,50).

Specific Reports on Silymarin's Nephroprotective Impact in Paracetamol-Induced Nephrotoxicity

Gopi *et al*. conducted a 14-day trial in which paracetamol toxicity was generated in male rats for the first three days with a dosage of 500 mg/kg body weight (BW)/day orally, followed by silymarin administration from day four to fourteen through oral gavage at a dose of 25 mg/kg BW/day. Post-treatment with silymarin provided renal and hepatic protection against paracetamol poisoning, as evidenced by lower renal biomarkers of injury such as BUN and SCr and a significant decrease in serum hepatic biomarkers such as AST, total cholesterol (TC), and triglyceride levels (TG) (51).

Silymarin has been shown in a study conducted by Abd Ellah *et al*. to have nephroprotective effects in preventing paracetamol-induced nephrotoxicity in rats. These effects are linked to silymarin's capacity to reduce oxidative and nitrosative stress in renal tissue as well as to enhance mitochondrial energy production. Before high acute dose of oral paracetamol intoxication (3000 mg/kg BW), rats were pretreated with oral silymarin supplementation (200 mg/kg BW/day) for nine days. Silymarin increased serum total protein and creatinine clearance, decreased renal tissue LPO as shown by a decrease in thiobarbituric acid reactive substance (TBARS), nitrate content, and an increase in renal tissue antioxidant enzymes, as well as a normalization of renal tissue adenosine triphosphate (ATP) content (52).

Earlier research by Ramachandran *et al*. revealed that silymarin's ability to preserve kidneys comes from its ability to reduce the oxidative stress of paracetamol-induced oxidative stress. They discovered that silymarin 25 mg/kg BW, given orally for six days following a single intraperitoneal

paracetamol (750 mg/kg BW) administration in male rats restored antioxidant molecule levels in kidney tissues, including superoxide dismutase (SOD), catalase (CAT), GSH, and glutathione peroxidase (GPx), as well as reduced renal tissues TBARS levels (53).

Shelbaya attempted to examine the preventive effect of milk thistle aqueous extract against paracetamol-induced toxicity in female rats. Paracetamol (200 mg/kg BW/day) and milk thistle extract (500 mg/kg BW/day orally) were given to the animals simultaneously for 60 days. The administration of paracetamol significantly disrupted the lipid profile, of the hepatic, and renal functions, but the co-administration of paracetamol with milk thistle extract established the renal protection, anti-hyperlipidemia, and hepato-cardio protection, as evidenced by a large drop in serum urea and SCr, an improvement in the lipid profile, an increase in antioxidant enzymes, and a reduction in the hepatic biomarker of injury (54).

The protective properties of silymarin on the hepato-renal system were studied in an experimental rat model. Three days of intraperitoneal intoxication with 500 mg/kg BW/day of paracetamol were administered to the animals. Silymarin is administered orally at a dose of 10 mg/kg BW/day for five days before the introduction of paracetamol and continues through day six. Silymarin's hepatoprotective effects were demonstrated by a decrease in serum liver enzymes and an increase in total proteins, whilst its nephroprotective effects were demonstrated by a decrease in serum electrolytes, blood urea, and creatinine. Additionally, the non-protein sulfhydryl moiety in liver and kidney tissues increased due to silymarin's actions, and both organs' histopathological deteriorations improved (55).

A further study by Hamza and Al-Harbi discovered that post-treatments of adult mice with silymarin at a dose of 50 mg/kg BW/day for 30 consecutive days following an acute oral dose of paracetamol (2 g/kg BW) led to improvements in kidney function as evidenced by a significant decrease in serum urea and SCr, an improvement in the anti-oxidative state of the renal tissues as shown by an increase in antioxidant enzymes like CAT and SOD and decreasing LPO indicated by low malondialdehyde (MDA) concentrations (56).

Adil and colleagues evaluated the preventive benefits of silymarin against the oxidative damage to rats' liver and kidneys brought on by prolonged paracetamol intake. They discovered that silymarin 25 mg/kg BW/day administered by gavage two hours before paracetamol 700 mg/kg BW for 14 days considerably raised body weights and serum albumin, while dramatically lowering BUN, SCr, serum liver enzymes, and total bilirubin levels compared to the paracetamol group. Additionally, silymarin administration demonstrated antioxidant activity as seen by an increase in the levels of antioxidant agents in the liver and kidney tissues, including SOD levels and renal GSH but not hepatic GSH, as well as a substantial decrease in MAD and nitric oxide. Additionally, silymarin attenuated the histopathological changes in both organs due to paracetamol toxicity (57).

Furthermore, silymarin may protect the liver and kidney from damage caused by paracetamol due to its antioxidant and anti-inflammatory capabilities, according to research by Bektur *et al*. In this study, female mice were given a single intraperitoneal injection of paracetamol (500 mg/kg BW) followed by seven days of oral silymarin treatment (100 mg/kg BW/day). This led to normalization of body weight,

histopathological damage, serum hepatic enzymes and BUN and SCr, and nitric oxide (NO) levels in liver and kidney tissues (58).

Dinar and colleagues used a New Zealand rabbit model to study the nephroprotective effects of silymarin against paracetamol-induced kidney damage. When the animals received oral silymarin 100 mg/kg BW/day for 14 days before receiving a single oral dosage of 600 mg/kg BW of paracetamol, their levels of blood liver enzymes, urea, and creatinine were much lower than when they received paracetamol alone suggesting nephroprotective properties of silymarin (38).

Another research supports the hepato-renal protective effects of silymarin (100 mg/kg BW/day, orally for 30 days) pretreatment of rats before acute toxicity caused by 2 g/kg BW of paracetamol. In comparison to the intoxicated group, silymarin pretreatment dramatically decreased blood levels of liver enzymes, urea, and creatinine. It also improved the antioxidant status of the liver and kidney tissues as shown by a considerable increase in SOD, CAT, and a decrease in MDA, as well as histopathological abnormalities (59).

In research by Onaolapo *et al*. on rats, silymarin was given orally for 14 days at a dosage of 25 mg/kg BW/day, followed by a three-day intraperitoneal paracetamol (800 mg/kg BW/day) intoxication. This study hypothesized that silymarin pretreatment might prevent paracetamol-induced hepatic, renal, and neurological damage. As well, the anti-oxidant status has improved, and histological analysis of the tissues shows varying degrees of tissue protection (60).

The hepatic and renal protective effects of silymarin were validated in another investigation by Ali *et al*. in rats pretreated with silymarin (100 mg/kg BW/day, p.o. for 30 days) before receiving oral paracetamol (500 mg/kg BW/day, for seven days). Silymarin showed protective benefits by reducing blood levels of bilirubin, urea, uric acid, creatinine, and low-density lipoprotein cholesterol. Furthermore, compared to the paracetamol-controlled group, there was a substantially higher total protein and high-density lipoprotein cholesterol level. Histopathological results and decreased LPO peroxidation in the liver and kidneys further supported the hepatoprotective benefits (61).

Based on histology and biochemical findings, silymarin enhanced kidney protective actions have been reported by Simon *et al*. They discovered that silymarin pretreatment (100 mg/kg BW/day) for eight days before acute paracetamol poisoning (2 g/kg BW) resulted in significantly higher levels of SOD and GSH, significantly lower levels of MDA in renal tissues, and significantly lower levels of serum urea and SCr. Furthermore, silymarin was found to lessen the cellular damage caused by paracetamol in a histological analysis (62).

In another study, Ahmad and Zeb found that male mice given silymarin 100 mg/kg BW/day after receiving paracetamol 300 mg/kg BW/day for two weeks showed no significant differences in serum albumin, total serum protein, or blood biochemical like serum urea and serum creatinine compared to untreated control animals. Also, it has positive benefits with increased levels of GSH in renal tissues and a considerable drop in TBARS levels compared to mice treated with paracetamol (63).

According to research by Al-Asmari and colleagues, silymarin pre-treatment for 14 consecutive days before an acute high paracetamol dose (1000 mg/kg BW) reduced the severity of hepatic and extra-hepatic lesions brought on by the paracetamol high dose, shown by a considerable decrease in blood liver enzymes, an improvement in

serum lipid profile, a change in renal function parameters (a decrease in SCr, urea, and uric acid), a decrease in serum electrolytes, and a better state of histopathological changes. Moreover, silymarin pretreatment modified paracetamol-induced oxidant/antioxidant disparity in hepatic and renal tissues by diminishing the increase of MDA and increasing of non-protein sulfhydryl compared to the intoxicated group (64).

In a separate study, Salman *et al*. found that co-administration of paracetamol (750 mg/kg BW/day, orally) and silymarin (50 mg/kg BW/day, orally) for 30 days protected rats' kidneys from the potentially harmful effects of paracetamol as evidenced by a drop in serum urea and creatinine levels compared to paracetamol-only treated animals (65).

In research by Quyamuddin *et al*. rats were given silymarin oral doses of 100 mg/kg BW/day for ten days before being intoxicated with paracetamol 750 mg/kg BW/day for three days for an additional ten days. Silymarin substantially lowered blood urea, SCr, and elevated serum uric acid and total protein as compared to the paracetamol-impaired group. Moreover, the level of antioxidant enzymes in renal tissue was greatly recovered. These discoveries may represent a possible nephroprotective drug against kidney damage (18).

A recent study performed by Abd EL Latif *et al*. demonstrated that silymarin's anti-inflammatory and anti-oxidant effects protect against paracetamol-induced hepatic and renal toxicity. Female rats were pretreated with silymarin 100 mg/kg BW/day orally for seven consecutive days before they received an acute paracetamol dosage of 2 g/kg BW. Silymarin treatment resulted in lower levels of serum urea, Scr, bilirubin, and liver enzymes. Additionally, a better redox state in the liver and kidney tissues was demonstrated by levels of CAT rising and MDA falling (66).

Additionally, a recent study by Simon *et al*. showed that silymarin had hepato-renal protective effects in female rats given silymarin 25 mg/kg BW and paracetamol 900 mg/kg BW intraperitoneally. When compared to animals given paracetamol, silymarin therapy resulted in a significantly lower level of blood liver enzymes, total cholesterol, urea, creatinine, and uric acid. Also, compared to the paracetamol group, the histological image revealed reduced inflammation (67).

CONCLUSION:

This review concludes that paracetamol overdose, acute or chronic, adversely affects kidney function. Based on the outcomes of animal studies, Silymarin therapy may have protective or mitigating effects against drug-induced kidney injury, notably against damage caused by paracetamol. Silymarin's nephroprotective effects are related to its antioxidant, anti-inflammatory, and cell membrane stabilizing properties.

CONFLICT OF INTEREST: There is no conflict of interest.

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