



## Original Article

Determine the Curing Effects of *Silybum marianum* (milk thistle) Administered Orally to Non-Alcoholic Fatty Liver Disease (NAFLD) Patients for Six MonthsAqsa Qurban<sup>1</sup>, Hamid Khan<sup>2</sup>, Fizza Ali<sup>1</sup>, Saba Abbas<sup>3</sup>, Syeda Amber Hameed<sup>4</sup> and Nousheen Hussain<sup>5</sup><sup>1</sup>Department of Life Sciences, University of Management and Technology, Lahore, Pakistan<sup>2</sup>Department of Biochemistry, Quaid-E-Azam University, Islamabad, Pakistan<sup>3</sup>Department of Microbiology, Government College University Faisalabad, Pakistan<sup>4</sup>Department of Microbiology, Ghazi National Institute of Engineering and Sciences, Dera Ghazi Khan, Pakistan<sup>5</sup>Quaid-E-Azam Medical College, Bahawalpur, Pakistan

## ARTICLE INFO

## Key Words:

NAFLD Patients, *S. marianum* (Milk Thistle), Ultrasound Technology, Hepatitis, Herbal Therapy

## How to Cite:

Qurban, A. ., Khan, H. ., Ali, F. ., Abbas, S. ., Hameed, S. A. ., & Hussain, N. . (2023). Determine the Curing Effects of *Silybum marianum* (milk thistle) Administered Orally to Non-Alcoholic Fatty Liver Disease (NAFLD) Patients for Six Months: Curing Effects of *Silybum marianum*. *Pakistan BioMedical Journal*, 6(04).<https://doi.org/10.54393/pbmj.v6i04.869>

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[aqsaqurban22@gmail.com](mailto:aqsaqurban22@gmail.com)Received Date: 15<sup>th</sup> March, 2023Acceptance Date: 19<sup>th</sup> April, 2023Published Date: 30<sup>th</sup> April, 2023

## ABSTRACT

*Silybum marianum* is the scientific name of milk thistle. For centuries, it is used to treat hepatitis, cirrhosis, jaundice, diabetes, and indigestion. The bioactive agents of milk thistle contain Apigenin, silybin, betaine, free fatty acids, silybin, silychristin, and silidianin. **Objective:** To determine the potential of *Silybum marianum* (milk thistle) in non-alcoholic fatty liver disease patients. **Methods:** It was a cross-sectional and experimental based study with NAFLD patients. A significant age range of 30 to 60 years was chosen for the 40 patients (20 men and 20 women). Screening period after liver biopsies (before and after the use of one capsule of *S. marianum* (Silymarin Standardize milk Thistle 300mg/day metabolic maintenance). Ultrasound technology assessed the liver condition at the start of the study and after the herbal 6-months therapy. **Results:** Out of 40 patients, 10 (25%) had hyperlipidemia and 5 (12.5%) were diabetics. The results of the 6-month therapy research study showed that the blood AST and ALT levels of NAFLD patients had significantly decreased. The average ALT and AST baseline concentrations were 85 and 65.9IU/ml, respectively. AST value (before and after therapy) showed a statistically significant difference in 80% of the NAFLD patients treated with *S. marianum* (32 out of 40; p=0.007). With a p-value of 0.05, alanine transaminase (ALT) normalization of disease severity was accomplished in 65% of patients (26 out of 40 patients). **Conclusions:** The therapy of NAFLD via *S. marianum* is successful in terms of biochemical improvement, especially when other medications have failed or when used in conjunction with other therapeutic techniques.

## INTRODUCTION

Milk thistle seeds (*Silybum marianum*) has been used for more than 2000 years as a curing agent for many illnesses exclusively liver diseases. The milk thistle originated from Southern Europe, Asia Minor, and North Africa. It has now become a common weed and cultivated plant in Europe, Africa, the Americas, and Australia [1, 2]. The white patterns (variegation) on the leaves, which have been used as a vegetable, are the reason of giving milk thistle as its name [3]. Roasted seeds have been used as a replacement for coffee. The mature, untreated seeds of milk thistle have been used in traditional medicine for 2000 years to cure

depression, headaches, digestive and liver issues, detoxification, and encourage breastfeeding. A modified form of milk thistle is Silymarin, also known as silydianin as a whole, which is a standardized extract that is sold and used commercially. Milk thistle seed powder components, especially silibinin, function as antioxidants and hepatoprotectives [1, 4, 5]. It is found successful in treating liver cirrhosis, fibrosis, gallbladder disease, and toxin poisoning. They also promote liver regeneration [6, 7]. Nonalcoholic fatty liver disease (NAFLD) is a clinic-pathologic illness characterized by considerable lipid

deposition i.e., more than 5% of the liver weight is deposited as triglycerides in the liver parenchyma of NAFLD patients [8]. It is estimated that 20–30% of the Western population possessed [9]. The pathophysiology of NAFLD is yet unclear, and empirical treatment is used to treat this illness. Even if there hasn't always been a benefit to losing weight, NAFLD may get better with it. Human research on the treatment of alcoholic cirrhosis and hepatitis is conflicting, nevertheless. The lipid, biliary, immunomodulatory, and anti-inflammatory properties of milk thistle seed. Other therapeutic qualities include antiviral, anticancer, and others. Milk thistle medicines are risk-free, well-tolerated, and have no significant adverse effects [4, 10, 11]. The current study compared the effectiveness and safety of *Silybum marianum* when given orally to NAFLD patients for three months.

## METHODS

It was a cross-sectional research-based study conducted among patients with NAFLD visited Sheikh Zaid Hospital in the region of Lahore. 40 patients (n=20 males and 20 females) were selected having a considerable age range of 30–60 years. Liver biopsies during the screening period were carried out to rule out alternate causes of liver diseases and to prove the histologic diagnosis of NAFLD. The primary indicator was the persistent elevation of ALT and AST. After an attempt to control the metabolic circumstances and after six or more months of follow-up which indicated fatty liver biopsies during the screening period via the intake of one capsule of *S. marianum* (Silymarin Standardize milk Thistle 300mg/day metabolic maintenance). At the beginning of the trial and the conclusion of the treatment, the liver was evaluated using ultrasound technology. The updated criteria were used in the ultra-sonographic examination to identify fatty liver. The patients were followed up with a weight-reducing diet for at least three months and reported a higher amount of alanine aminotransferase (ALT) values were included in this group. Patients who used more than 20g of ethanol per day were disqualified. By monitoring alanine aminotransferase (ALT) readings, the patients were monitored while on a weight-reduction regimen for at least three months. Raw data regarding socio-demographic aspects of NAFLD patients obtained from the survey of 40 patients was carried out by using SPSS software (version 22.0). ALT and AST levels were found by using 95% accuracy using a two-sided p-value of 0.05. baseline and population comparisons were undertaken using student t-tests and chi-squared tests for equal proportions. A p-value of 0.05 was considered significant.

## RESULTS

40 candidates (n=20 males and n=20 females) with a mean

age value of  $48.25 \pm 12.3$  were selected for this current study. No patient had reported clinical cirrhosis or malignant liver. In our study, there were no patients with a BMI higher than 40 were included. Results showed that out of 40 patients, 5 (12.5%) were diabetics and 10 (25%) reported hyperlipidemia (Table 1).

**Table 1:** Socio-demographic aspects of NAFLD patients

Parameters	<i>S. marianum</i>
Age	35.9 ± 10
Gender (F/M)	20/20
BMI	44.8 ± 9.3
Diabetics	5 (12.5%)
Hyperlipidemia	10 (25%)

The research study of this 6-month's therapy session demonstrated a notable decline in the serum AST and ALT concentrations in NAFLD patients. In the study groups, the average baseline serum ALT and AST concentrations were  $85\mu$  10IU/ml and  $65.9\mu$  10IU/ml, respectively. Alanine transaminase (ALT) normalization was achieved in 65% of patients (26 out of 40 patients) with a p-value of 0.05. 80% of NAFLD patients (32 out of 40) treated with *S. marianum*, showed statistically significant difference in AST value (before and after therapy) ( $p=0.007$ ) (Table 2).

**Table 2:** Clinical values before and after 6 months of therapy with one capsule of *S. marianum* (Silymarin Standardize Milk Thistle 300mg/day metabolic maintenance)

Parameter	Baseline ALT level (IU/ml) (Initial)	ALT normalization N (%)	Baseline AST level (IU/ml) (After 6 months)	AST normalization n (%)
<i>S. marianum</i>	$85\mu$ 10IU/ml	26/40 (65%) ( $p=0.05$ )	$65.9\mu$ 10IU/ml	32/40 (80%) ( $p<0.007$ )

## DISCUSSION

The presence of fatty acids in human blood is produced by dietary lipid intake, lipolytic adipose tissue activity, and fatty acid synthesis [12]. According to the current study's findings, a 7% weight loss (average 6.6 kg) is associated with a considerable reduction in the degree of liver steatosis and an improvement in biochemical indicators. There was a substantial drop in AST, ALT, and insulin levels, as well as insulin resistance among those people [13]. Many studies have demonstrated the connections between NAFLD and *Silybum marianum* and highlighted the fact that insulin resistance, and metabolic syndrome, a loss in physical activity, an increase in weight, and changes in eating habits might all be triggering the progression of NAFLD [14–17]. Oxidative stress is considered to be responsible for the majority of hepatocyte lipid accumulation, hepatic inflammation, and fibrosis. Similar findings were also reported by. For lowering fibrosis and inflammation or delaying the course of NAFLD, there is not enough solid data to support any treatment interventions [4]. However, to delay the progression of the illness, weight

loss, and anti-oxidant medications may be necessary [18, 19]. Our current 6-month treatment research study revealed that there was a noticeable decrease in the blood AST and ALT values of NAFLD patients. The average baseline levels of ALT and AST in the study groups were 85 and 65.9 IU/ml, respectively. 80% of NAFLD patients (32 out of 40) treated with *S. marianum* exhibited a statistically significant difference in AST value (before and after therapy) ( $p=0.007$ ). Alanine transaminase (ALT) normalization was achieved in 65% of patients (26 out of 40 patients) with a p-value of 0.05 [20]. Another research study suggested the treatment of NAFLD patients with *S. marianum* and vitamin E is well-tolerated and safe. Each instance finished the research, and patient medication adherence was good in both groups [21]. Other research studies also have employed the use of vitamin E and *Silybum marianum* as antioxidants to defend the liver against toxins [22]. They have been researched for use of anticarcinogen as a supportive therapy for liver damage brought on by poisoning with *Amanita phalloides*. The active component of the *S. marianum*, silybin, has a variety of distinct hypothesized mechanisms of action, although the main one is still unknown [23]. *S. marianum* is thought to have antioxidant properties since it increases the activity of superoxide dismutase in lymphocytes and erythrocytes. It is also considered to note that *S. marianum* also helps in the development of the hepatocyte membrane, preventing toxins from entering the cell through enterohepatic recirculation, and aiding in liver regeneration by boosting ribosomal protein synthesis and activating nucleolar polymerase A. Previous study by Del Ben et al., suggested *S. marianum* would be useful in treating NAFLD were either uncontrolled or conducted on a wide range of people with fatty liver. There are rare research studies available for NAFLD management. The bulk of studies on the treatment of NAFLD emphasizes the improvement of concomitant diseases such as obesity, diabetes mellitus, and hyperlipidemia [24].

## CONCLUSIONS

The therapy of NAFLD via *S. marianum* is successful in terms of biochemical improvement, especially when natural medications have prioritized or when used in conjunction with other liver therapeutic techniques. The cost of milk thistle seed *S. marianum* therapy is the lowest of any therapy, and its side effects are hardly noticeable. Our findings are need to be verified in more extensive research with pre-and post-treatment biopsies in the future.

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