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**ORIGINAL ARTICLE**

# Analyze the Efficacy of Silymarin in Treating Newly Diagnosed Cases of Type 2 Diabetes Mellitus by Contrasting its Effects on Glycemic Control and Insulin Resistance

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## ABSTRACT

**Objective:** The purpose of this research was to examine the efficacy of Silymarin in treating newly diagnosed cases of type II diabetes mellitus (T2DM), specifically with regard to glycemic control and insulin resistance.
**Study design:** An observational, randomized, placebo- controlled study.
**Place and duration:** Medicine department of Dr. Akbar Niazi Teaching Hospital (ANTH), Islamabad for the duration from August 2021 to January 2022.
**Methods**: The sixty individuals with a recent diagnosis of type 2 diabetes were chosen at random. There were a total of 60 patients, split evenly between 2 groups of 30. For 90 days, those in Group A took a silymarin capsule containing 200 mg, whereas those in Group B had a placebo capsule looking very similar to the real thing. Fasting blood glucose (FBG), random blood glucose (RBG), glycated haemoglobin A1C (A1C), fasting insulin (FI), and homeostasis model assessment of insulin resistance (HOMA-IR) were measured before and after therapy. The data was examined after 90 days. Statistical analysis was performed using SPSS-20.0. If the probability value was less than 0.05, it was considered significant. The Chi-squared test was employed for statistical analysis.
**Results**: Mean age of the patients of group A (silymarin) was 50.5 years while mean age of group B (controlled) patients was 51.0 years. In both the groups, females were more in numbers as 80% in silymarin group and 70% in controlled group. There was no significant difference showed on the basis of age, gender, BMI, education, family history and employment. Silymarin therapy for 12weeks improved the levels of RBG, RBG, HbA1c, FSI and HOMA-IR. A significant difference p-value<0.001 was showed in these variables between the two groups at baseline and after 90days treatment.
**Conclusion**: The treatment of Silymarin supplementation of 200mg three time a day for newly diagnosed type II diabetic patients had a beneficial effect on improving the blood glucose levels and decreased insulin resistance as compared to standard treatment alone.

## INTRODUCTION

An extract of the fruit of the Silybum marianum (L.) Gaertn. plant, silymarin is a combination of active flavonolignans and flavonoids. The use of silymarin for the treatment of liver disorders is quite ancient. A variety of pharmacologically active molecules can be found in silymarin, with flavonolignans and flavonoids standing out [1]. Chemically speaking, silymarin has anti-inflammatory actions [2, 3] and acts as a scavenger for free radicals [2]. Today, it is used to treat type 2 diabetes (T2D) [5] and a variety of liver illnesses characterised by chronic inflammation [4, 5].

Globally, 8.3% of the population has diabetes, or an estimated 382 million individuals [6]. The prevalence of diabetic mellitus (T2DM) has skyrocketed in recent years and is now considered a global pandemic. Type 2 diabetes is the fourth greatest cause of mortality in industrialised nations [7] due to the two- to fourfold higher risk of coronary heart disease and stroke. Both in the United States and Europe, diabetes is the major cause of end-stage renal disease (ESRD) and the need for dialysis [8]. Nephropathy affects around 20%-30% of diabetic people. Ever more individuals are being diagnosed with diabetes, putting a heavy financial strain on the healthcare system [9]. It was anticipated in 2012 that this cost would reach $245 billion in the United States alone.

Patients, doctors, and healthcare systems everywhere face a major obstacle in tackling diabetes management. There is an immediate need for more effective treatment alternatives to prevent and slow the worsening of diabetes-related problems. Finding innovative treatments for diabetic nephropathy requires looking outside the realm of traditional pharmaceuticals and into the realm of complementary and alternative medicine.

Silibinin is the active component, and it helps reduce insulin resistance (IR). It is recognised that insulin resistance exists prior to the development of type 2 diabetes [10], which is significant since IR is connected to a wide variety of liver diseases. IR is highly associated with overweight and obesity. In addition, persistent inflammation is connected to insulin resistance in obese states. Obesity is one of the primary contributors to inflammation, which plays a significant part in the development of insulin resistance (IR) [11]. According to a number of studies, an improvement in insulin sensitivity can be observed in non-fat cells when TNF levels in fat cells decrease. Internal kinases such as cd36 kinase (JNK) and I kappa B kinase complex (IKK) become active in response to the presence of TNF. By phosphorylating serine residues on diabetes substrate 1, these kinases inhibit the substrate's ability to bind to the receptor. the increased involvement of transcription factors An uptick in pro-inflammatory cytokine production is associated with obesity due to upregulation of the transcriptional factors activator protein 1 (AP-1) or Nuclear protein kappa of activated B cells (NF-kB). Inflammatory response (IR) is increased when adipose tissue releases cytokines into the circulation, leading to a rise in overall total level of pro-inflammatory substances with endocrine effects in the muscles and liver [12].

Silymarin, the active element in milk thistle (Silybum marianum (L.) Gaertn. ), is a polyphenolic flavonolignan with putative antioxidant activities. It consists of four flavonolignans isomers—silybin, isosilybin, silydianin, and silychristin—and one flavonoid, taxifolin [13]. Among the flavonolignans, silymarin may have antioxidant effects. Studies conducted in both vitro and in vivo have indicated that silymarin and the elements that make up silymarin have a broad variety of biological actions, some of which include an anti-inflammatory and antioxidant impact. These biological effects are supposedly the basis for the purported therapeutic potential of silymarin in the treatment of diabetes [14]. It helps with a broad variety of illnesses in addition to its anti-cancer, anti-atherosclerotic, pro, and renoprotective qualities.

Additionally, it is useful in the treatment of burns and sepsis [15, 16], as well as in the prevention of Alzheimer's disease.

This research aimed to compare the efficacy of adding silymarin supplementation therapy to conventional antidiabetic treatment in newly diagnosed type II diabetes mellitus patients with respect to glycemic control and insulin resistance.

## MATERIAL AND METHODS

The present study was observational, randomized placebo-controlled study conducted on 60 adult patients with newly diagnosed type II diabetes mellitus. The study was conducted in the department of medicine, Dr. Akbar Niazi Teaching Hospital (ANTH), Islamabad for the duration from August 2021 to January 2022. Each subject gave written consent after being instructed on the study's methodology.

Participants in this study ranged in age from 40 to 66, and all had been recently diagnosed with type 2 diabetes mellitus and had less-than-ideal glycemic control. Patients with severe liver disorders, renal insufficiency, severe heart dysfunction, a history of myocardial infarction, malignancy, mental health disease, severe infections, breastfeeding or pregnancy, taking other herbal or multivitamin -mineral supplements, smoking, corticosteroids use during in the study, experienced any changes in their medications during the study period, and use of P-glycoprotein antagonists were not eligible for participation.

Random selection was used to choose sixty individuals who had just been diagnosed with type 2 diabetes. The 60 patients were divided into two groups, each consisting of 30 people. The participants in Group A took a silymarin capsule daily that included 200 milligrammes of the herb, whereas the participants in Group B got a placebo capsule that was the same size and form as the silymarin capsule. Before and after therapy, the following parameters were evaluated: blood sugar ( fbs (FBG), random blood glucose (RBG), glycated haemoglobin (HbA1c), fast insulin (FI), and homa assessment (HOMA-IR). After keeping an eye on them for ninety days, they were investigated. In addition, the Homeostasis Model Evaluation of Insulin Resistance (HOMA-IR) was calculated based on the values of the patients' fasting glucose and fasting insulin using the formula HOMA-IR = FPG (mg/dL) FSI (U/mL)/405. This formula was used to estimate the patients' insulin resistance. SPSS-20.0 was used to do the analysis on the data. In this investigation, a level of statistical significance was determined to exist when the p-value was lower than 0.05. In the course of this inquiry, we carried out a statistical test known as the Chi-square test.

## RESULTS

Total sixty patients were enrolled in this study. Out of which thirty were male and thirty were females and they were randomly distributed in the two groups of 30 each: Group A (Silymarin) and Group B (Controlled). There were 6(20%) males and 24(80%) females in group A while in group B there were 9(30%) males and 21(70%) females. Age of patients ranged from 40 t0 66. Mean age of patients in group A was 50.5 and in group B mean age was noticed as 51.0. Patients in both the groups showed BMI as 34.2 and 33.7kg/$M^2$. Literacy rate was 50% in both groups. 18 patients in group A and 21 patients in group B had family history with this disease. Hence, there was no significant difference among the two groups on the basis of age, gender, education, employment, family history, and body mass index (BMI).(table 1)

Table 1: Patient's clinical and demographic aspects

| Variables | Group A (Silymarin) n=30 | % | Group B (Controlled) n=30 | % |
|---|---|---|---|---|
| Age (years) | 50.5 | | 51.0 | |
| Gender | | | | |
| Male | 6 | 20 | 9 | 30 |
| Female | 24 | 80 | 21 | 70 |
| Education | | | | |
| Literate | 15 | 50 | 15 | 50 |
| Illiterate | 15 | 50 | 15 | 50 |
| Mean BMI(kg/$M^2$) | 34.2 | | 33.7 | |
| Family history | | | | |
| Yes (+) | 18 | 60 | 21 | 70 |
| No (-) | 12 | 40 | 9 | 30 |
| Employment | | | | |
| Employed | 15 | 50 | | 55 |
| Unemployed | 15 | 50 | | 45 |

After Silymarin supplementation therapy of 90days, there showed a significant difference in HbA1c, FBG and FSI levels among the two groups at the baseline and at the end of the treatment. (Table 2)

Table 2: Outcomes among both groups

| Variables | Group A | Group B |
|---|---|---|
| Mean Fasting blood glucose (mg/dl) | | |
| At baseline | 317.4±11.24 | 318.4±11.24 |
| After 90-days | 183.8±7.41 | 245.9±10.38 |
| Mean Random blood glucose (mg/dl | | |
| At baseline | 317.4±11.24 | 317.4±11.24 |
| After 90-days | 182.8±7.41 | 247.9±10.38 |
| Mean A1C (%) | | |
| At baseline | 8.6±7.17 | 8.4±10.38 |
| After 90-days | 6.17±1.12 | 7.4±5.25 |
| Mean Insulin resistance (HOMA-IR | | |
| At baseline | 4.3±2.14 | 4.7±5.30 |
| After 90-days | 1.1±0.12 | 1.9±3.19 |

## DISCUSSION

Reducing insulin resistance, silymarin was found to be an effective glucose regulator. Silymarin's anti-diabetic action has been postulated to work through a few different mechanisms, which has piqued the interest of those working in the field of diabetes treatment and complications. In-vivo and in-vitro investigations have previously demonstrated the therapeutic potential of Silymarin and its derivatives [17]. It has been found that silymarin has antioxidant, anti-inflammatory, anti-gluconeogenesis, and membrane-stabilizing properties. There is evidence that both insulin gene expression and beta-cell proliferation occur. Silymarin acts like an agonist on the peroxisome proliferator-activated receptor-alpha (PPAR). Based on the aforementioned data, silymarin seems to have great anti-diabetic potential. Our results are consistent with the aforementioned research, documenting silymarin's beneficial effect on glycemic management and its potential to reduce insulin resistance. [18]

In our study 60 patients were presented. Patients were equally divided in two groups. Mean age of the patients of group A (silymarin) was 50.5 years while mean age of group B (controlled) patients was 51.0 years. In both the groups, females were more in numbers as 80% in silymarin group and 70% in controlled group. There was no significant difference showed on the basis of age, gender, BMI, education, family history and employment. These were comparable to the previous studies.[19]

The levels of fasting blood glucose, recurrent blood glucose, a1c, FI, and HOMA-IR were all considerably reduced by the silymarin in the current investigation, compared to the control group. Given the rising prevalence of diabetes mellitus (DM) in the country and the potential anti-diabetic benefits of silymarin, the results of the present investigation have important clinical implications. Additionally, a previous study[20] bolsters the anti-diabetic potential of Silymarin by reporting optimal glycemic control in T2DM subjects who were given a 200 mg dose of Silymarin three times daily in addition to glibenclamide for 120 days. This study's results on A1C are very consistent with those of the previous one, which found that it was low relative to baseline. Previous research[21] in diabetics with alcoholic cirrhosis using 600 mg of silymarin daily found reductions in fasting blood glucose, glycated hemoglobin, and fasting insulin. There is evidence that silymarin's polyphenolic compounds can improve the glycemic and lipid profiles of type 2 diabetics. [22] Study18 used silymarin at 140

mg three times daily for 45 days in type 2 diabetics and reported positive effects on glycemic and lipid profile. Insulin resistance can be decreased, which accords with earlier research. [23-25] Improvements in fasting insulin (FI) and homeostasis model assessment (HOMA-IR) are of major therapeutic importance.

While the aforementioned literature lends credence to the results of the current study, it is clear that more research is needed, ideally involving a sizable sample of the indigenous community. Future, large prospective studies are needed to more fully explore the beneficial effects of silymarin on glycemic management and insulin resistance.

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