



## Investigation the Antioxidant Features and Therapeutic Potential of Onion Peel Husk on Elevated Liver Enzymes with Induced Liver Fibrosis in Male Albino Rats

Kiran Aslam<sup>1</sup>, Qura-tul-ain<sup>1</sup>, Aqsa Farooq<sup>2</sup>, Maham Saeed<sup>3</sup>, Hafiza Nimra Mukhtar<sup>3</sup>, Arooj Fatima<sup>1</sup>, Sidra Habib<sup>3</sup>, Menahil Azmat<sup>3</sup>

<sup>1</sup>Government Graduate College of Home Economics, Faisalabad, Punjab, Pakistan..

<sup>2</sup>Department of Nutritional Sciences, Government College Women University, Faisalabad, Punjab, Pakistan.

<sup>3</sup>Department of Nutrition and Dietetics, The University of Faisalabad, Punjab, Pakistan.

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**Corresponding Author:** Kiran Aslam, Government Graduate College of Home Economics, Faisalabad, Punjab, Pakistan. Email: [kiranasm@gmail.com](mailto:kiranasm@gmail.com)

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### ABSTRACT

Liver inflammations and fibrosis can be due to liver injury. In liver fibrosis, inflammations which trigger myofibroblasts in the liver release extracellular matrix proteins that produce fibrous scar. There exist a number of plants which are helpful in regulating the malfunctioning of liver enzymes in liver fibrosis. Onion peel contains quercetin which is effective against the management of malfunctioning liver enzymes. 15 albino male subjects were induced with liver fibrosis using carbon tetrachloride injection to investigate their elevated liver function enzymes when given different doses of red onion peel. The serum level of alanine transaminase and aspartate transaminase enzymes were investigated. While members of treatment groups I (T1) and II (T2) received ROP powder in encapsulated quantities of 150 mg and 300 mg per kilogram of body weight, respectively, for 15 days, members of the control group (T0) received no therapy. Onion peel powder can be useful in treating malfunctioning liver enzymes in caused liver fibrosis, as seen by the significant decrease in liver enzymes seen in treatment groups. All results were taken significantly at  $p < 0.05$ .

### INTRODUCTION

Liver inflammations and fibrosis can be due to liver injury. In liver fibrosis, inflammations which trigger myofibroblasts in the liver release extracellular matrix proteins that produce fibrous scar. The hepatic stellate cells that live there are the main source of these myofibroblasts (Kisseleva, T. and Brenner, D., 2021). Hepatic fibrogenesis, a pathologic result of chronic liver injury, is typified by an abnormal accumulation of extracellular matrix proteins. The dynamic process of fibrosis involves interactions between invasive and local immune cells, hepatic stellate cells, sinusoidal endothelial cells, and hepatic parenchymal cells (hepatocytes). This study focuses on the main cell types that cause liver fibrosis, the cytokines and chemokines that affect this process, and the conditions that must be met for fibrosis to reverse (Dhar and associates, 2020). One of the biggest worldwide health concerns is liver fibrosis, which can be brought on by either metabolic or

viral chronic liver disorders. Since fibrosis is linked to the development of liver disease, it is crucial to both the course of the sickness and the risk of developing hepatocellular carcinoma (HCC). Despite variations in basic liver damage mechanisms and disease-specific cell responses, the development of fibrotic liver disease exhibits comparable patterns across the main liver disease aetiologies. The scientific understanding of the processes of liver fibrosis has changed significantly during the last 10 years (Roehlen, N., et al., 2020). Hepatic fibrogenesis, a pathologic result of chronic liver injury, is typified by an abnormal accumulation of extracellular matrix proteins. The dynamic process of fibrosis involves interactions between invasive and local immune cells, hepatic stellate cells, sinusoidal endothelial cells, and hepatic parenchymal cells (hepatocytes).

There exist a number of plants which are helpful in regulating the malfunctioning of liver enzymes in liver fibrosis. Onion peel is one of the plants which contain vital therapeutic agents. Its flavor is very distinctive, resembling leeks or garlic as well as onions. Moreover, they have been used traditionally as medicines for their ability to reduce inflammation, oxidation, and pain, especially when it comes to hepatoprotective properties. Its flavor is very distinctive, resembling leeks or garlic as well as onions. Moreover, they have been used traditionally as medicines for their ability to reduce inflammation, oxidation, and pain, especially when it comes to hepatoprotective properties (Jiang, Y.C., et.al., 2022). The study investigated the therapeutic potential of red onion peel powder against malfunctioning liver enzymes in induced liver fibrosis in rats.

## MATERIAL AND METHODS

### Collection and Preparation of Raw Material

After being gathered at the neighborhood market, red onions were peeled off. The peel was cleared of any dirt and debris. Additionally, 70% alcohol was used to clean them before being rinsed with distilled water that had been disinfected. After being dried overnight at 50 °C in a lab hot air oven, it was finely milled into powder using an electric grinder (El-Beltagi et al., 2022). According to El-Shazly et al. (2017), this refined red onion peel (ROP) powder was kept at room temperature in airtight containers. Milk thistle doses were encapsulated in gelatin capsules, which were determined to be safe for human consumption after being obtained from Halal capsule Pvt. Ltd (Touchette & Cox, 2022).

### Chemical Characterization of Red Onion Peel

#### Phytochemical Features of Red Onion Peel

Methanol extraction was used to determine the red onion peel's total phenolic content (TPC) and total flavonoid content (TFC). M'hiri et al. (2015) state that the amount of TPC and TFC was stated in milligrams of quercetin equivalents (QE) per gram of the dry weight of the sample.

### Investigation Effect of Red Onion Peel on Elevated Liver Enzymes Male Albino Rats with Induced Toxicity

#### Procurement and Handling of Animals

The National Institute of Health (NIH), located in Islamabad, provided 15 male wistar albino rats that were 10 weeks old and weighed between 200 and 220 grams. Rats were housed in glass cages in an animal house and supplied water and food at will. The animal home has a 12-hour cycle of light and dark.

#### Induction of Liver Fibrosis

To induce liver fibrosis in rats, 5 mg of carbon tetrachloride were injected into the body of rats (Chhimwal, J., et.al., 2020).

## Study Design

The study was conducted for 8 weeks from 1st to 15th December 2022.

## Treatment Plan

Three groups of five subjects each were created. Oral gavage was used to provide the dose.

**Table I**

*Treatment Groups and Treatment Plan*

| Treatment Groups | Title             | Treatment  |
|------------------|-------------------|--|
| G <sub>0</sub>   | Control           | No treatment                                       |
| G <sub>1</sub>   | Treatment group 1 | Red onion peel powder 150 mg per kg of body weight |
| G <sub>2</sub>   | Treatment group 2 | Red onion peel powder 3000 mg kg of body weight    |

## Liver Function Enzymes test

Liver functioning enzymes ALT and AST were measured before and after 8 weeks of trial (Ni et al., 2012).

## Statistical Analysis

The degree of significance ( $p < 0.05$ ) was examined utilizing a fully randomized design (CRD) and descriptive statistical analysis with the independent sample t-test. The findings were displayed as mean  $\pm$  S.D. IBM SPSS Statistics 20 was used for all statistical analyses.

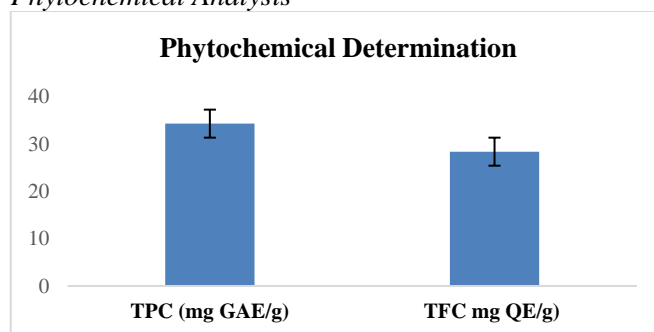
## RESULTS

The purpose of this study was to ascertain the phytochemical content, and enzymes that measure changes in liver function were examined.

### Phytochemical Characters of Red Onion Peel POP carried a significant amount of TPC and TFC depicted in Figure I.

**Figure 1**

*Phytochemical Analysis*



### Investigation Effect of Red Onion Peel on Elevated Liver Enzymes in Induced Liver Fibrosis

In order to examine their raised liver function enzymes when administered varying dosages of ROP, 15 male albino subjects were injected with carbon tetrachloride to produce liver fibrosis. The levels of the enzyme's aspartate transaminase and alanine transaminase in the serum were examined. While members of treatment groups I (T1) and II (T2) received ROP powder in encapsulated quantities of 150 mg and 300 mg per

kilogram of body weight, respectively, for 15 days, members of the control group (T<sub>0</sub>) received no therapy.

### Changes in Alanine Transaminase Levels

The findings showed a substantial reduction in the elevated blood alanine transaminase levels in both treatment groups. While group II's ALT levels dropped from 43.58±8.23 U/L to 29.34±17.85\* U/L, group I's dropped from 45.63±9.86 U/L to 34.21±16.74\* U/L. However, compared to the 0-day, the control group's ALT levels increased somewhat on the 15th day.

**Table 2**

*Mean ± S.D. for Changes in ALT levels in U/L*

| Duration             | T <sub>0</sub> | T <sub>1</sub> | T <sub>2</sub> | p-value |
|----------------------|----------------|----------------|----------------|---------|
| 0 day                | 43.25±10.25    | 45.63±9.86     | 43.58±8.23     | p<0.05  |
| 45 <sup>th</sup> day | 44.28±10.87    | 34.21±16.74*   | 29.34±17.85*   | p<0.05  |

T<sub>0</sub> = No Treatment, T<sub>1</sub>=Red onion peel powder 150 mg per kg of body weight, T<sub>2</sub>=Red onion peel powder 300 mg per kg of body weight.

### Changes in Aspartate Transaminase Levels

Results showed significant reduction in elevated serum aspartate transaminase levels in both treatment groups. Group-I showed a reduction in AST levels from 67.63±9.86 U/L to 59.28±18.74\* U/L while group II showed a reduction in AST levels from 63.58±8.23 U/L to 56.34±17.85\* U/L. However, the control group showed a slight increase in AST levels on the 15<sup>th</sup> day as compared to the 0-day.

**Table 3**

*Mean ± S.D for Changes in AST levels in U/L*

| Duration             | T <sub>0</sub> | T <sub>1</sub> | T <sub>2</sub> | p-value |
|----------------------|----------------|----------------|----------------|---------|
| 0 day                | 61.25±10.25    | 67.63±9.86     | 63.58±8.23     | p<0.05  |
| 45 <sup>th</sup> day | 61.28±10.87    | 59.28±18.74*   | 56.34±17.85*   | p<0.05  |

T<sub>0</sub> = No Treatment, T<sub>1</sub>=Red onion peel powder 150 mg per kg of body weight, T<sub>2</sub>=Red onion peel powder 300 mg per kg of body weight.

## DISCUSSIONS

The purpose of the study was to look at how ROS affected the liver enzymes in rats that had liver fibrosis. To examine their enhanced liver function enzymes when administered varying dosages of ROP, albino male participants were injected with carbon tetrachloride to produce liver fibrosis. The serum level of alanine transaminase and aspartate transaminase enzymes were investigated. A study that investigated the effect of purple onion on induced toxicity reported improvement in liver function enzymes. The current study investigated

superoxide's possible defenses against toxicity-induced liver damage. For one week, SO or silymarin was given orally to BALB/c mice. After that, carbon tetrachloride (CCl<sub>4</sub>) was injected to cause hepatic fibrosis. The effect of SO against hepatic fibrosis was evaluated by analyzing the liver tissue for apoptosis, cytokine levels, extracellular matrix, oxidative stress, serum transaminase, and histological alterations. Raw 264 supernatant was used to incubate HSC-T6 cells in a plate. Following LPS priming of seven cells, SO extracts or Niclosamide (a STAT3 inhibitor) were introduced at the proper intervals and doses. SO regulated the balance of ECM, including -SMA, collagen-I, and TIMP-1, and decreased serum transaminase levels and oxidative stress in animals induced by CCl<sub>4</sub>. SO reduced the positive expression of -SMA and NLRP3 by blocking STAT3 phosphorylation in activated HSCs. Depending on the STAT3 signaling pathway, SO may have health-promoting benefits for liver dysfunction by reducing hepatic fibrogenesis, apoptosis, and inflammation in the formation of hepatic. Another study examined the effects of onion peel quercetin (OPQ) on oxidative stress, liver function, and steatosis in mice given ethanol and found improvements in liver function enzymes. Mice administered OPQ and silymarin showed significantly lower blood levels of ALT, AST, and ALP than mice given ethanol (P 0.05). Catalase activity was significantly greater in mice given 50 mg/kg OPQ than in controls (P 0.05). MDA levels were significantly higher than the controls' after OPQ therapy (P 0.05). Mice fed ethanol showed signs of hepatocyte damage, steatosis, and elevated lipid peroxidation. Compared to ethanol treatment, OPQ significantly reduced serum levels of ALP, ALT, and AST (N.I. Dibal et al., 2022).

## CONCLUSION

Milk thistle is the most widely researched plant and studies have proven the hepato-protective effect. Milk thistle contains flavanol lignans which is helpful in regulating the liver enzymes. Liver enzymes are not within normal ranges, are observed in people suffering from chronic hepatic diseases. Milk thistle has great potential in lowering these abnormally arisen liver enzymes and preventing the liver from damage. This study has proven that milk thistle seeds can improve liver condition and can be used as managerial therapy for liver diseases.

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