Original Research

Effect of *Momordica charantia* (bitter melon) on serum glucose level and various protein parameters in acetaminophen intoxicated rabbits

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Abstract

Aim: Liver function tests, including total plasma proteins, albumin, bilirubin and glucose were analyzed to find out the hepatocurative and hepatoprotective effects of *Momordica charantia*.

Method: The study was divided into two categories. In first category, the livers of rabbits were intoxicated with acetaminophen, and then *Momordica* fruit extract was given to observe its hepatocurative effects.

Results: The results indicated significant changes in concentrations of the parameters in acetaminophen-challenged rabbits. In the second category, treatment was started by giving *Momordica* fruit extract dose orally for 10 days and 15 days to two groups of rabbits, respectively. Then, livers of rabbits were damaged with acetaminophen and hepatoprotective effects of *Momordica* were observed.

Conclusion: The results showed that the animals treated with *Momordica* fruit extract experienced less liver damage due to acetaminophen intoxication, indicating that *Momordica* has hepatoprotective properties.

**INTRODUCTION**

Nutrigenomics has emerged as an important facet in current biology because of lesser tissue toxicity and off target effects. Various lines of evidence suggest utilization of plants with reference to their medicinal properties since the dawn of mankind. *Momordica charantia* or bitter melon has been used extensively in folk medicine as a remedy for diabetes [1, 2]. In the past decades, research has been focused on scientific evaluation of traditional drugs of plant origin. *Momordica charantia* is one such plant that has been frequently used as medicine [3]. *Momordica* has also been reported to show a wide range of biological activities including antioxidant, antiviral, antimicrobial, antiulcerogenic, anticancerous and antihapatotoxic activities [4, 5, 6, 7]. It has been found that this plant possesses effective components in preventing HIV [6]. The studies have also shown its efficacy in various cancers such as lymphoid leukemia, breast cancer, skin tumor, prostate cancer, squamous carcinoma of tongue and larynx [7].

Semiz & Sen found that *Momordica charantia* fruit extract was found to be containing free radical scavenging activity, which can exert a protective action against patho-physiological alterations caused by the presence of superoxide and hydroxide free radicals [8].

The liver diseases are constantly posing a challenge for human beings in the world at large. As liver is a major detoxifying and drug metabolizing organ of the body, therefore liver regulates many important metabolic functions. Hepatic injury is associated with distortion of these metabolic functions [9]. The diverse functional activity of the liver lends itself to the use of a number of different testing procedures. Multiple parameters are representatives of proper liver function. Of the substances released by damaged hepatic cells, enzymes and metabolites appearing in the blood are most useful...
as indicators of possible liver injury. Also, the excretion of chemicals removed from the circulation into the bile is used to detect and assess severity of the damage [10]. The signs and symptoms of drug-induced hepatotoxicities are similar to those of natural disease [11]. Acetaminophen (paracetamol) is an analgesic and antipyretic drug that, in large overdose, can cause liver necrosis in man and laboratory animals [12, 13].

This project was carried out to evaluate the pharmacological properties of *M. charantia* in respect to hepatic diseases, and also to search for cheaper and effective therapeutic agents to mask the symptoms and ultimately cure the liver diseases.

**MATERIALS AND METHODS**

**Plant Extract**

The freshly obtained fruits of *M. charantia* were washed and air-dried. The whole fruits along with seeds were macerated in electric mixer then soaked in water and stirred vigourously and left overnight. The mixture then filtered properly through sieve and the filtrate thus obtained was dried at reduced temperature.

**Animals**

Male rabbits (*Oryctolagus cuniculus*) weighing 1-2 kg were used for the study, purchased from veterinary center, Lahore. The animals were housed in the University Animal House to acclimatize in standard conditions and fed with standard diet and water.

**Experimental Design**

The study was divided in two categories.

**Hepatocurative Studies**

Five healthy rabbits were selected for the treatment. First blood sampling was done for control reading on day 0, normal values of liver function tests (LFTs) were recorded. To induce liver damage, acetaminophen was given for consecutive three days, the standard dose was 1500 mg/kg body weight, recommended by Kamran [14]. Blood was analyzed for LFTs on Day 3. Then from day 4 onwards, *Momordica charantia* fruit extract was given (5ml/ kg body weight), for 15 days on daily basis. Blood sampling was done at intervals, like on day 6, day 11, day 16, and day 20.

**Hepatoprotective studies**

This category was further divided into two phases,

**i) Hepatoprotective (P 10) studies**

This group consisted of five animals. Sampling of blood was done on day 0 for control reading. The treatment was started with the administration of *Momordica charantia* fruit extract daily (5 ml/kg body weight) from day 1 to day 10. After 10 days, the livers of rabbits were challenged with Acetaminophen (1500 mg/kg body weight) for three consectives days (11th to 13th day). Blood sampling was done on 13th and 16th day, and the changes in the concentrations of total plasma protein, albumin, bilirubin and blood glucose were observed.

**ii) Hepatoprotective (P 15) studies**

The group comprised five animals. For control reading, blood sampling on day 0 was done. In this category, *Momordica charantia* fruit extract daily (5 ml/ kg body weight) was given for 15 days from day 1 to day 15. Afterwards, the livers of rabbits were intoxicated with acetaminophen (1500 mg/kg body weight) for three consecutive days (16th to 18th day). Blood sampling was done on 18th and 21st day, and the changes in the concentrations of total plasma protein, albumin, bilirubin and blood glucose were observed.

**Blood Sampling**

The blood was collected from marginal ear vein of rabbit with 23/25 guage needle in the morning (8 am - 9am). It was centrifuged at 3500 rpm for 5 minutes to obtain the serum.

**Liver Function Tests (LFTs)**

The liver function tests, including, total plasma proteins, albumin, bilirubin and glucose were studied.

**Chemicals**

Acetaminophen was used as a hepatotoxic drug. LFT test kits for total plasma proteins, albumin and glucose by Audit diagnostics, Ireland and for bilirubin by Biocon Diagnostik, Germany, were used for serological analysis.

**Statistical Analysis**

The data was analyzed by using ANOVA (One-way Analysis of Variance). The probability less than 0.05 (P< 0.05) was considered as significant represented by asterisks in tables.

**RESULTS**

**Hepatocurative studies**

**Total plasma proteins**

Blood sampling was done on 0 day for control reading. The concentration of total plasma proteins in untreated (control) animal was 79.1 ± 0.79 g/l. After 3 days acetaminophen administration there was significant decrease in serum total protein levels (39.7 ± 0.76 g/l) indicating liver damage. Total protein concentrations were found to be significantly increasing after treatment with *M. charantia* extract. The values were, 57.2 ± 0.81, 62.7 ± 1.01, 66.2 ± 0.96, 73.2 ± 0.64 g/l for 6th, 11th, 16th, and 20th day readings, respectively (Table 1).
Variations among the concentrations of total plasma proteins, albumin, bilirubin and glucose during the hepatocurative treatment.

Table 1.

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Total Plasma Proteins (g/l)</th>
<th>Albumin (mg/dl)</th>
<th>Bilirubin (mg/dl)</th>
<th>Glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Day 0)</td>
<td>79.1 ± 0.79</td>
<td>8.8 ± 0.79</td>
<td>1.13 ± 0.22</td>
<td>138.17 ± 0.9</td>
</tr>
<tr>
<td>Acetaminophen (Day 3)</td>
<td>39.7 ± 0.76*</td>
<td>5.03 ± 0.98*</td>
<td>4.08 ± 0.54*</td>
<td>97.9 ± 0.322*</td>
</tr>
<tr>
<td>Momordica extract (Day 6)</td>
<td>57.2 ± 0.81*</td>
<td>6.35 ± 0.81*</td>
<td>3.73 ± 0.25*</td>
<td>92.21 ± 0.34*</td>
</tr>
<tr>
<td>Momordica extract (Day 11)</td>
<td>62.7 ± 1.01*</td>
<td>6.9 ± 0.02*</td>
<td>3.11 ± 0.09*</td>
<td>90.34 ± 0.4*</td>
</tr>
<tr>
<td>Momordica extract (Day 16)</td>
<td>66.2 ± 0.96*</td>
<td>7.4 ± 0.1*</td>
<td>1.92 ± 0.02*</td>
<td>90.05 ± 0.67*</td>
</tr>
<tr>
<td>Momordica extract (Day 20)</td>
<td>73.2 ± 0.64*</td>
<td>7.75 ± 0.24*</td>
<td>1.69 ± 0.24*</td>
<td>84.76 ± 0.33*</td>
</tr>
</tbody>
</table>

Albumin

During the hepatocurative treatment, blood sampling was done on 0 day, for control reading. The concentration of albumin in untreated (normal) animal was 8.8 ± 0.91 mg/dl. After three days of acetaminophen intoxication there was significant fall in serum albumin levels i.e. 5.03 ± 0.98* mg/dl indicating liver damage. Then afterwards, animals were treated with Momordica extract, albumin concentrations were found to be significantly increasing with that treatment. The values were, 6.35 ± 0.81*, 6.9 ± 0.02*, 7.4 ± 0.01*, 7.75 ± 0.24* mg/dl at 6th, 11th, 16th, and 20th day readings respectively (Table 1).

Bilirubin

Blood sampling was done on 0 day, for control reading. The concentration of bilirubin in untreated (normal) animal was 1.13 ± 0.22 mg/dl. After that, acetaminophen was administered for three days and there was significant elevation in total bilirubin levels i.e. 4.08 ± 0.54 mg/dl, showing liver damage. Then afterwards, animals were treated with Momordica extract, the bilirubin concentrations were found to be significantly decreasing with that treatment. The values were, 3.73 ± 0.25, 3.11 ± 0.09, 1.92 ± 0.02, and 1.69 ± 0.24 mg/dl for 6th, 11th, 16th, and 20th day readings respectively, indicated in Table 1.

Glucose

The concentration of blood glucose in untreated (normal) animal was 138.17 ± 0.9 mg/dl. After that, acetaminophen was administered and there was significant decrease in blood glucose levels i.e. 97.9 ± 0.322* mg/dl, after 3 days, showing liver damage. Then afterwards, animals were treated with Momordica extract, blood glucose concentrations were found to be significantly decreasing with that treatment. The values are, 92.21 ± 0.34*, 90.34 ± 0.4*, 90.35 ± 0.67*, 84.76 ± 0.33* mg/dl for 6th, 11th, 16th, and 20th day readings respectively. (Table 1)

Hepatoprotective (P 10) studies

Total plasma proteins

In hepatoprotective (P10) treatment the control (0 day) total plasma protein reading was 73.8 ± 1.3 g/l. After treatment with M. charantia extract (at day 10), total plasma protein reading was increased non-significantly (72.8 ± 1.1 g/l). There was a significant decrease in total plasma protein values i.e. 54.8 ± 1.65 and 51.5 ± 0.57 g/l in 13th day and 16th day sampling, respectively (Table 2).

Table 2. Variations among the concentrations of total plasma proteins, albumin, bilirubin and glucose during the hepatoprotective (P 10) treatment.

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Total Plasma Proteins (g/l)</th>
<th>Albumin (mg/dl)</th>
<th>Bilirubin (mg/dl)</th>
<th>Glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Day 0)</td>
<td>73.8 ± 1.3</td>
<td>8.3 ± 0.61</td>
<td>1.05 ± 1.8</td>
<td>136.62 ± 1.05</td>
</tr>
<tr>
<td>Momordica extract (Day 10)</td>
<td>72.8 ± 1.1</td>
<td>8.09 ± 0.09</td>
<td>1.08 ± 0.28</td>
<td>115.91 ± 0.96*</td>
</tr>
<tr>
<td>Acetaminophen (Day 13)</td>
<td>54.8 ± 1.65*</td>
<td>6.24 ± 0.86*</td>
<td>3.03 ± 0.43*</td>
<td>109.46 ± 0.44*</td>
</tr>
<tr>
<td>Acetaminophen (Day 16)</td>
<td>51.5 ± 0.57*</td>
<td>5.37 ± 1.2*</td>
<td>4.12 ± 0.85*</td>
<td>110.99 ± 0.46*</td>
</tr>
</tbody>
</table>

http://www.jicep.com
Table 3. Variations among the concentrations of total plasma proteins, albumin, bilirubin and glucose during the hepatoprotective (P15) treatment.

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Total Plasma Proteins (g/l)</th>
<th>Albumin (mg/dl)</th>
<th>Bilirubin (mg/dl)</th>
<th>Glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Day 0)</td>
<td>75.6 ± 1.09</td>
<td>8.72 ± 0.23</td>
<td>1.01 ± 1.22</td>
<td>136.04 ± 0.12</td>
</tr>
<tr>
<td>Momordica extract (Day 15)</td>
<td>75.3 ± 1.13</td>
<td>8.6 ± 1.12</td>
<td>0.98 ± 1.65*</td>
<td>104.22 ± 0.85*</td>
</tr>
<tr>
<td>Acetaminophen (Day 18)</td>
<td>62.6 ± 0.75*</td>
<td>7.4 ± 0.95*</td>
<td>2.31 ± 0.45*</td>
<td>107.54 ± 1.3*</td>
</tr>
<tr>
<td>Acetaminophen (Day 21)</td>
<td>54.9 ± 0.89*</td>
<td>6.18 ± 0.56*</td>
<td>3.67 ± 0.87*</td>
<td>111.86 ± 0.55*</td>
</tr>
</tbody>
</table>

Albumin

The control (0 day) albumin reading was 8.3± 0.61 mg/dl. After treatment with *M. charantia* extract (at day 10), albumin reading was increased non-significantly (8.09 ± 0.09 mg/dl). After that, the animals were challenged with acetaminophen. There was a fall observed in albumin value i.e. 6.24 ± 0.88* and 5.37±1.2* mg/dl in 13th day and 16th day sampling, respectively (Table 2).

Bilirubin

In hepatoprotective (P10) treatment the control (0 day) bilirubin reading was 1.05±1.8 mg/dl. Then during the treatment *Momordica* extract was administered into the animals. The value of bilirubin concentration was found to be 1.08±0.28 mg/dl. After that, the animals were challenged with acetaminophen. A rise was observed in bilirubin value i.e. 3.03±0.43* and 4.12±0.85* mg/dl in 13th day and 16th day sampling (Table 2).

Glucose

The control reading for blood glucose was 136.62±1.05 U/l. Then *Momordica* extract was given to the animals and the value of blood glucose concentration was found to be 115.91±0.96* mg/dl. After that, the animals were challenged with acetaminophen. There was a fall observed in bilirubin value i.e. 109.46±0.44* and 110.99±0.46* mg/dl in 13th day and 16th day sampling, after the liver damage, but the values were high as compared to the hepatocurative liver damage, showing that there is some protective properties in the extract (Table 2).

Hepatoprotective (P15) studies

Total plasma proteins

In hepatoprotective (P15) treatment the control (0 day) total plasma protein reading was 75.6 ± 1.09 g/l. After treatment with *M. charantia* extract (at day 15), total plasma protein reading was 75.3 ± 1.13 g/l. After that, the animals were challenged with acetaminophen. There was a fall observed in total plasma protein levels in serum i.e. 62.60 ± 0.75 and 54.9 ± 0.89 g/l in 18th day and 21st day sampling, after the liver damage, but the values were high as compared to the hepatocurative liver damage, showing that there are some protective properties in the extract. (Table 3).

Albumin

Similarly in hepatoprotective (P15) treatment The control (0 day) albumin reading was 8.72±0.23 mg/dl. Then during the treatment *Momordica* extract was administered into the animals. The value of albumin concentration was found to be 8.6±1.12* mg/dl. After that, the animals were challenged with acetaminophen. There was a decrease in albumin value i.e. 7.4 ± 0.95* and 6.18 ± 0.56* mg/dl in 13th day and 16th day sampling, after the liver damage (Table 3).

Bilirubin

The control (0 day) bilirubin reading was 1.01±1.22 mg/dl and then *Momordica* extract was administered into the animals at of 5ml/kg body wt. The value of bilirubin concentration was found to be 0.98±1.65* mg/dl. Afterwards, the animals were challenged with acetaminophen. There was a rise observed in bilirubin value i.e. 2.31±0.45* and 3.67±0.87* mg/dl in 13th day and 16th day sampling, after the liver damage, as indicated in Table 3.

Glucose

The control (0 day) blood glucose reading was 136.04 ± 0.12 mg/dl. Then during the treatment *Momordica* extract was administered into the animals. The value of glucose concentration was found to be 104.22 ± 0.85* mg/dl. After that, the animals were challenged with acetaminophen. There was a increasing trend observed in blood glucose value i.e. 107.54 ± 1.3* and 111.86 ± 0.55* mg/dl in 13th day and 16th day sampling (Table 3).
DISCUSSION

The effect of Momordica fruit extract was experimentally evaluated during the current study. The parameters included Liver function tests like, total plasma proteins, albumin, bilirubin and Glucose concentrations in blood. For the induction of experimental hepatotoxicity, acetaminophen (paracetamol) was used. When therapeutic doses of acetaminophen are given, this metabolite is quickly metabolized to a non-toxic derivative by glutathione [15] and excreted in the urine as conjugates of cysteine and mercaptopuric acid. However overdose of paracetamole causes the damage to the liver [13]. When acetaminophen is taken in large doses or has been used long-term, the glucuronic acid or sulphate pathways become saturated and an increased amount of acetaminophen is metabolized by the cytochrome P-450 system to form the toxic metabolites. Glutathione conjugation increases but the amount of glutathione available is limited. Once the supply of glutathione becomes depleted, N-acetyl p-benzoquinoneimine binds covalently and irreversibly to hepatic cellular protein macromolecules and causes cell damage and death of hepatocytes [16, 17,18].

In this study we found that M. charantia brings the altered levels of total plasma proteins, albumin and bilirubin of acetaminophen intoxicated mice to their normal levels. Our work correlates to Dandagi and coworkers who explore the hepatoprotective activity of various extracts of Ferula asafoetida, M. charantia and Nardosta jatamansi against experimental hepatotoxicity and the results demonstrated that the extracts of Momordica charantia Linn. have significant hepatoprotective activity [19]. The hepatoprotective role of Momordica extract in our findings seems to be due to enhanced antioxidant enzymes these enzymes have the capability to engulf reactive oxygen species that can damage the liver [20]. In another study by Chaudhri et. al, also found hepatoprotective activity of hydro-alcoholic extract of M. charantia leaves by estimation of SGOT, SGPT, ALP and total Bilirubin [20]. Similar results have been reported for some other ethnobotanical fruits and herbs [21, 22, 23].

In conclusion, the results of the present study indicate that the M. charantia fruit extract have both hepatoprotective (protect liver from injuries) and hepatocurative (Cures the injured liver) properties. Further studies are needed to see if a higher dose and different routes of administration of M. charantia have a hepatoprotective effect.

REFERENCES

glycyrrhizinate in drug induced liver injury An M Phil Thesis submitted to Faculty of Pharmacy, University of Punjab, Lahore, Pakistan. 2002.


