Abstract:

This study aimed to find out the possible effect of downy mildew infection of lettuce plants in powder form on experimental rats. Thirty adult white male rats, each weighing (110-140) g, were used and divided into 5 equal groups (sex rats in each group). The first group is the negative control group. As for the other groups, healthy and infected lettuce leaves were added, used at a rate of 5% and 10% each of the main meal in crushed form. At the end of the experiment, they were anesthetized and blood samples were collected and body weight gain, feed intake, Feed Efficiency Ratio, liver functions (GPT - GOT - ALP), kidney functions (urea - creatinine - uric acid), total protein, (albumin - globulin), blood lipid level (total cholesterol - triglycerides), lipoproteins (HDL-c - LDL-c - VLDL-c) and complete blood count (hemoglobin - hematocrit - platelets - RBCs - WBCs) were evaluated. Histopathological examination of the liver and kidney was also performed. The obtained results concluded that feeding on lettuce leaves led to a significant increase in (hemoglobin, hematocrit, platelets and red blood cells) and a decrease in (albumin, uric acid, urea, creatinine, white blood cells and liver and kidney weight) compared to the negative control group. Also feeding on 5% of infected lettuce leaves gave the highest value in...
Keywords: Biological evaluation – Lipid profile – Complete blood count – Liver and kidney functions - Histopathological Changes.

The potential impact of Downy Mildew

(Bremia Lactucae) on Lactuca Sativa

The study aimed to determine the potential impact of Downy Mildew infection on the blood picture of rats.

The experiment was conducted on 30 rats divided into two groups: a control group consisting of 15 rats and an experimental group consisting of 15 rats. The control group was fed normal diet, while the experimental group was fed a diet containing 5% of the infected leaf mixture.

The following blood tests were performed:

- Hemoglobin
- Hematocrit
- Platelets
- Red blood cells
- Albumin
- Uric acid
- Creatinine
- White blood cells
- Liver and kidney functions (GPT – GOT – ALP)
- Histopathological changes

The results showed a decrease in hemoglobin, hematocrit, and platelets, and an increase in albumin, uric acid, creatinine, and white blood cells.

The keywords for this study are: biological evaluation, lipid profile, complete blood count, liver and kidney functions, and histopathological changes.
Introduction:

Lettuce (*Lactuca sativa, L*) belongs to the Asteraceae family and originates in the Mediterranean. Due to the minimal processing procedures, such as cutting, washing, drying, packing, and low-temperature distribution and storage, fresh-cut lettuce maintains its nutritional value and bioactivity. Additionally, the findings demonstrated that the consumption of lettuce preserved in modified-atmosphere packaging did not alter the plasma redox state of healthy participants (*Serafini et al., 2002*).

Additionally, phytochemical compositions and contents are different in various types. Compared with green lettuce and red lettuce, some studies have reported that red lettuce has comparatively higher phenolic levels than green. Thus, red lettuce is a good source of antioxidants in the daily diet (*Wilson et al., 2004*).

Lettuce is a successful and diverse plant distributed worldwide. The first cultivated lettuce appears in several primitive writings in early 2680 BCE as a medicinal herb. The Asteraceae can be considered the family of plants with a large number of species, around 23,000 to 30,000 (*Funk et al., 2005*). In Asian countries, lettuce and asparagus lettuce are traditionally cooked rather than consumed raw (*Mou, 2009*). Consuming lettuce is beneficial for human health related to the bioactive compounds in vegetables (*Coria-Cayupán et al., 2009*).

Natural antioxidant compounds extracted and identified from plant sources such as lettuce have become a popular trend because of the general awareness of the importance of a healthy diet and limitations on the use of hazardous synthetic antioxidants (*Vázquez et al., 2012*).

The neurological properties of lettuce are another health aspect of lettuce and detailed research in recent times has proved the anxiolytic properties of lettuce in vivo. In an experimental animal model, for lettuce extract fed animals, locomotive activity was found to be reduced, suggesting significant anxiolysis (*Komaki et al., 2014*).

Formally, there are seven different types in the lettuce group, including Cos (Romaine), Butterhead, Leaf, Stalk (or Asparagus), Crisphead (Iceberg), Latin, and Oilseed. The whole heads of lettuce and the fresh-cut form are the common products in the market. The colors, shapes, and nutrients are important factors to affect consumer purchase choice (*Mampholo et al., 2016*).

Lettuce, a low-calories, low-fat, and low-sodium salad
vegetable, is rich in fiber, folate, and vitamin C, as well as essential minerals such as iron. It is also an abundant source of other natural health-promoting phytochemicals and vitamins, including glycosylated flavonoids, hydroxycinnamic acids, sesquiterpene lactones (lactucin and lactucopicrin), carotenoids, the group B vitamins, ascorbic acid, and tocopherols. Lettuce secondary metabolites are potentially associated with many health-beneficial properties, including antifree radical, anti-inflammatory, antidiabetic, anticancer, and anti cardiovascular diseases (CVDs) effects (Kim et al., 2016).

Lettuce (Lactuca sativa, L) is one of the most frequently consumed vegetable crop species globally. The modern types of cultivated lettuce are categorized based on their huge diversity in morphological features and are mainly classified as crisphead, butterhead, romaine, looseleaf, or stem lettuce (Zhang et al., 2016).

Lettuce is commercially accessible year-round and grown in open fields, greenhouses, or the plant factory with artificial light systems (PFALs). The annual global production of lettuce (and chicory) is 27.2 million tons; China, the United States of America, India, Spain, and Italy are the top five producers (USDA, 2012).

Lettuce is an important natural source of phytochemicals. These molecules, which include glycosylated flavonoids, phenolic acids, carotenoids, vitamin B groups, ascorbic acid, tocopherols, and sesquiterpene lactones, are vital bioactive nutritional components (Uddin et al., 2020 and Mitra et al., 2021). It was found that lettuce contains a high amount of Vitamin C (Medina-Lozano et al., 2021).

Furthermore, several researchers found that hydroponic Lactuca sativa can heal diseases such as oxidative damage, cancer, Alzheimer’s disease, and diabetes (Bahbah et al., 2021 and Naseem and Ismail, 2022).

Lettuce is rich in water with 94–95% content and low in calories. It is also an excellent source of vitamins, minerals, and bioactive compounds such as polyphenols, carotenoids, and chlorophyll with related health benefits (Yang et al., 2022).

The lettuce downy mildew, caused by the biotrophic oomycete Bremia lactucae, is one of the main diseases of lettuce crop, because it reduces the quality of the leaves - the marketable part of the crop and is often accentuated by post-harvest losses, which occur during transport and storage (Kunjeti et al., 2016 and Parra et al., 2016).

Symptoms of lettuce downy mildew usually occur as pale-yellow, angular patches delineated by the veins of the leaves. On the abaxial side of the leaves, the presence of white sporangia, consisting of
sporangiophores and sporangia is observed (Mieslerová et al., 2013).

The disease management of lettuce downy mildew is mainly done through fungicide application and use of resistant cultivars, carrying Dm genes or resistance factors R, which express hypersensitivity reaction (Castoldi et al., 2014 and Tobar-Tosse et al., 2017).

Materials and Methods:

Materials:
The used plants:

Lettuce Leaves (Lactuca sativa, L) were obtained from local market in shebin El-kom.

Rats:

Thirty adult male albino rats, weighing 110-140g from Medical Insects Research Institute, Doki, Cairo, were used in this study.

Rats were housed in wire cages under the normal laboratory condition and were fed on standard diet for a week as an adaptation period. Diet was offered to rats in special food cups to avoid looser conditions of food, water was provided to the rats by glass tubes supported to one side of the cage, food and water provided adlabium and checked daily.

Methods:

Preparation of materials:

All healthy lettuce leaves and infected with downy mildew were ground to give a powder after being sun-dried separately (Rojano-Aguilar et al., 2017) and kept in dark glass vials in a cool, dry and dark place to reduce oxidation of their contents until they are used.

Biological experiments:

Basal diet composition of tested rats:

Table (A): The composition of standard (basal) diet.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>10%</td>
</tr>
<tr>
<td>Corn oil</td>
<td>10%</td>
</tr>
<tr>
<td>Mineral Mixture</td>
<td>4%</td>
</tr>
<tr>
<td>Vitamin Mixture</td>
<td>1%</td>
</tr>
<tr>
<td>Cellulose</td>
<td>5%</td>
</tr>
<tr>
<td>Choline chloride</td>
<td>0.2%</td>
</tr>
<tr>
<td>Methionine</td>
<td>0.3%</td>
</tr>
<tr>
<td>Corn starch</td>
<td>Up to 100% (79.5%)</td>
</tr>
</tbody>
</table>

Experimental design:

The experiment was done in the Faculty of Home Economics, Menoufia University, Shebin El-kom. Rats were housed in wire cages in a room temperature 25°C and kept under normal healthy conditions.

Rats were divided into the following groups:

Group (1): Negative control group- normal group- (6 RATS), In this group rats were kept on standard diet and tap water.

Group (2): (6 RATS) Normal Rats were fed on healthy lettuce leaves powder at a concentration of 5% of the basal diet.

Group (3): (6 RATS) Normal Rats were fed on healthy lettuce leaves powder at a concentration of 10% of the basal diet.

Group (4): (6 RATS) Normal Rats were fed on infected lettuce leaves powder at a concentration of 5% of the basal diet.

Group (5): (6 RATS) Normal Rats were fed on infected lettuce leaves powder at a concentration of 10% of the basal diet.

Blood Sampling And Organs:

Blood samples were collected after 12 hours fasting at the end of the experiment using the abdominal aorta in which the rats were scarified under ether anethetized. Blood samples were received in to clean dry centerfuge tubes and left to clot at room temperature, then centerfuged for 10 minutes at 3000 rpm to separate the serum. Serum was carefully aspirate, transferred in to clean cuvet tubes, and stored frozen at -20°C for analysis. All serum samples were analyzed for determination the following parameters:

Lipid profile / cholesterol, total cholesterol (T.C), triglycerides (T.G), high density lipoprotein (H.D.L-C), low density lipoprotein (L.D.L-C), very low density lipoprotein (V.L.D.L-C), urea, creatinin, uric acid, glotamic oxaloacetic transaminas (G.O.T), glotamic pyruvic transaminas (G.P.T), and alkaline phsphatase (A.L.P).

At the same time, the organs: kidney and liver were removed, washed in salin solution, dried by filter paper, weighted, and stored frozen in formalin solution 10% for histopathological testing according to method mentioned by Drury and Wallington (1980).
Analytical Methods:

The following techniques were used for determination of different parameters in serum.

**Estimation of serum lipid:**

**Triglycerides:**

Enzymatic calorimetric determination of triglycerides was carried out according to Fassati and prencipe (1982).

**Total cholesterol:**

The principle use of total cholesterol determination according to Allen (1974).

**HDL-cholesterol:**

HDL can be determined by the same method used for total cholesterol, according to Lopez (1977).

**VLDL and LDL-cholesterol:**

The determination of VLDL (very low density lipoproteins) and LDL were carried out according to the method of Lee and Nieman (1996) as follows:

\[
\text{VLDL-c (mg/dl)} = \frac{\text{Triglycerides}}{5} \\
\text{LDL-c (mg/dl)} = (\text{Total cholesterol} - \text{HDL}) - \text{VLDL}
\]

**Determination of renal functions:**

**Estimation of urea:**

Urea was determined according to the enzymatic method of Patton and Crouch (1977).

**Estimation of creatinine in serum:**

Creatinine was determined according to kinetic method of Henry (1974).

**Determination of Uric acid:**

The intensity of this red color formed is proportional to the uric acid concentration in the sample (Schultz, 1984).

**Determination of liver functions:**

**Determination of serum alkaline phosphates (Alp):**

Enzymatic calorimetric determination of alkaline phosphates was carried out according to Belfield and Goldberg (1971).

**Estimation of serum glutamic oxaloacetic transaminases (GOT) and glutamic pyruvic transaminase (GPT):**
GOT and GPT activities were measured according to method described by Yound (1975) and Tietz (1976).

**Histopathological Investigation:**

Small specimens from liver and kidney were collected from all experimental groups, fixed in 15% neutral buffered formalin, dehydrated in ascending concentration of ethanol (70, 80, and 90%), cleared in xylene and embedded in paraffin. Sections of (4 - 6) μm thickness were prepared and stained with Hematoxylin and Eosin according to Bancroft et al., (1996).

**Statistically analysis:**

The data were statistically analyzed using a computerized costat program by one way ANOVA. The results are presented as mean ± SD. Differences between treatments at (P < 0.05) were considered significant (Snedecor and Cochran, 1967).

**Results and discussion:**

**Changes of total cholesterol (TC) and triglycerides (TG) level of normal rats fed on diet supplemented with lettuce leaves:**

Data tabulated in Table (1) show the changes of total cholesterol level of normal rats fed on diet supplemented with lettuce leaves. It is clear to mention that the total cholesterol level of control negative group recorded the highest value when comparing with other groups. The mean values were 140.35 , 85.24 , 88.58 , 73.52 and 92.49 mg/dl , respectively. There is non significant difference among the groups 2 , 3 and 5 but there is significant difference with the groups 1 and 4.

Also, Data presented in Table (1) show the changes of triglycerides level of normal rats fed on diet supplemented with lettuce leaves. It could be observed that the total triglycerides level of control negative group recorded the highest value when comparing with groups 2, 3 and 5, the lowest value when comparing with group 4 with significant differences. The mean values were 77.75 , 65.29 , 59.45 , 54.7 and 85.81 mg/dl, respectively.
Table (1): Changes of total cholesterol (TC) and triglycerides (TG) level of normal rats fed on diet supplemented with lettuce leaves

<table>
<thead>
<tr>
<th>Variables</th>
<th>(G1) Negative control</th>
<th>(G2) Healthy lettuce leaves 5%</th>
<th>(G3) Healthy lettuce leaves 10%</th>
<th>(G4) Infected lettuce leaves 5%</th>
<th>(G5) Infected lettuce leaves 10%</th>
<th>L.S.D (P ≤ 0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC level (mg/dl)</td>
<td>140.35 ± 7.85</td>
<td>85.24 ± 1.817</td>
<td>88.58 ± 1.945</td>
<td>73.52 ± 5.990</td>
<td>92.49 ± 2.81</td>
<td>8.629</td>
</tr>
<tr>
<td>% change of negative</td>
<td></td>
<td>-39.266</td>
<td>-36.886</td>
<td>-47.614</td>
<td>-34.100</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG level (mg/dl)</td>
<td>77.75 ± 2.257</td>
<td>65.29 ± 1.850</td>
<td>59.45 ± 3.745</td>
<td>85.81 ± 4.797</td>
<td>54.7 ± 2.57</td>
<td>5.877</td>
</tr>
<tr>
<td>% change of negative</td>
<td></td>
<td>-16.025</td>
<td>-23.529</td>
<td>10.374</td>
<td>-29.646</td>
<td></td>
</tr>
<tr>
<td>control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means in the same row with different litters are significantly different.

Changes of high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein (VLDL) level of normal rats fed on diet supplemented with lettuce leaves:

Data tabulated in Table (2) show the changes of high density lipoprotein level (HDL-c) of normal rats fed on diet supplemented with lettuce leaves. It is clear to notice that the high density lipoprotein level of control negative group recorded the highest value when comparing with other groups. The mean values were 47.30, 46.77, 46.69, 40.53 and 46.44 mg/dl, respectively. There is non significant difference between the groups 1, 2, 3 and 5 but there is significant difference with the group 4 when comparing with other groups. Data presented in Table (2) show the changes of low density lipoprotein level (LDL-c) of normal rats fed on diet supplemented with lettuce leaves. It could be observed that the low density lipoprotein level of control negative group recorded the highest value when comparing with other groups. The mean values were 77.50, 25.41, 29.99, 15.82 and 35.11 mg/dl, respectively. There is non significant difference among the groups 2, 3 and 5 while there is
significant difference with the groups 1 and 4. Also, Data given in Table (2) show the changes of very low density lipoprotein level (VLDL-c) of normal rats fed on diet supplemented with lettuce leaves. The obtained data indicated that the very low density lipoprotein level of control negative group recorded the highest value when comparing with groups 2, 3 and 5, the lowest value when comparing with group 4 with significant differences. The mean values were 15.54, 13.05, 11.89, 10.93 and 17.16 mg/dl, respectively.

Table (2): Changes of high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein (VLDL) level of normal rats fed on diet supplemented with lettuce leaves:

<table>
<thead>
<tr>
<th>Variables</th>
<th>(G1) Negative control</th>
<th>(G2) Healthy lettuce leaves 5%</th>
<th>(G3) Healthy lettuce leaves 10%</th>
<th>(G4) Infected lettuce leaves 5%</th>
<th>(G5) Infected lettuce leaves 10%</th>
<th>L.S.D (P ≤ 0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±SD</td>
<td>47.30 ± 1.190</td>
<td>46.77 ± 1.185</td>
<td>46.69 ± 2.998</td>
<td>40.53 ± 2.790</td>
<td>46.44 ± 1.502</td>
<td>3.8035</td>
</tr>
<tr>
<td>% change of negative control</td>
<td>-1.120</td>
<td>-1.283</td>
<td>-14.305</td>
<td>-1.824</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL-C level (mg/dl)</td>
<td>77.50 ± 8.135</td>
<td>25.41 ± 0.779</td>
<td>29.99 ± 3.541</td>
<td>15.82 ± 3.833</td>
<td>35.11 ± 2.268</td>
<td>8.1026</td>
</tr>
<tr>
<td>% change of negative control</td>
<td>-67.214</td>
<td>-61.304</td>
<td>-79.580</td>
<td>-54.694</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLDL-C level (mg/dl)</td>
<td>15.54 ± 0.45</td>
<td>13.05 ± 0.37</td>
<td>11.89 ± 0.75</td>
<td>17.16 ± 0.96</td>
<td>10.93 ± 0.517</td>
<td>1.1779</td>
</tr>
<tr>
<td>% change of negative control</td>
<td>-15.984</td>
<td>-23.487</td>
<td>10.424</td>
<td>-29.626</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means in the same row with different litters are significantly different.
Changes of GPT, GOT liver enzyme and ALP level of normal rats fed on diet supplemented with lettuce leaves:

Data given in Table (3) show the changes of GPT liver enzyme level of normal rats fed on diet supplemented with lettuce leaves. The obtained data indicated that the GPT liver enzyme level of control negative group recorded the highest value when comparing with groups 4 and 5, the lowest value when comparing with groups 2 and 3 with significant differences. The mean values were 84.02, 74.63, 61.80, 98.71 and 90.40 U/L, respectively. Data given in Table (3) show the changes of GOT liver enzyme level of normal rats fed on diet supplemented with lettuce leaves. The obtained data indicated that the GOT liver enzyme level of control negative group recorded the lowest value when comparing with other groups. The mean values were 27.07, 42.68, 79.30, 63.97 and 74.87 U/L, respectively. There is non significant difference among the groups 3 and 5 but there is significant difference between the groups 1, 2 and 4. Also, Data given in Table (3) show the changes of Alkaline Phosphatase (ALP) level of normal rats fed on diet supplemented with lettuce leaves. It could be noticed that the Alkaline Phosphatase (ALP) level of control negative group recorded the highest value when comparing with other groups. The mean values were 154.66, 124.13, 77.35, 92.69 and 78.18 U/L, respectively. There is non significant difference among the groups 3, 4 and 5 but there is significant difference between with the groups 1 and 2.

Table (3): Changes of GPT, GOT liver enzyme and ALP level of normal rats fed on diet supplemented with lettuce leaves:

<table>
<thead>
<tr>
<th>Variables</th>
<th>(G1) Negative control</th>
<th>(G2) Healthy lettuce leaves</th>
<th>(G3) Healthy lettuce leaves</th>
<th>(G4) Infected lettuce leaves</th>
<th>(G5) Infected lettuce leaves</th>
<th>L.S.D (P ≤ 0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
<td></td>
</tr>
<tr>
<td>GPT Level (U/L)</td>
<td>84.02b ± 3.1009</td>
<td>98.71a ± 5.215</td>
<td>90.40b ± 2.276</td>
<td>74.63c ± 3.580</td>
<td>61.80d ± 6.496</td>
<td>8.014</td>
</tr>
<tr>
<td>% change of negative Control</td>
<td>–</td>
<td>17.479</td>
<td>7.593</td>
<td>-11.175</td>
<td>-26.441</td>
<td></td>
</tr>
<tr>
<td>GOT</td>
<td>27.07d ±</td>
<td>42.68c ±</td>
<td>79.30a ±</td>
<td>63.97b ±</td>
<td>74.87a ±</td>
<td>10.094</td>
</tr>
</tbody>
</table>
Means in the same row with different litters are significantly different.

As regards to liver enzymes, results indicated that GPT levels (U/L) was significantly reduced when rats were fed on 5% or 10% infected lettuce leaves, whereas feeding rats on healthy lettuce leaves significantly caused an increase in GPT levels. However, feeding rats on 5% healthy lettuce leaves caused a significant reduction in GOT level in serum, whereas feeding rats on 5% infected lettuce leaves significantly reduced GOT level. Data revealed that feeding rats on 5% or 10% healthy leaves significantly caused a reduction in ALP level.

Also, feeding rats on healthy lettuce leaves significantly decreased TC and TG levels when compared to control negative group, whereas feeding rats on 5% infected lettuce leaves significantly increased Triglycerides in blood serum. Results indicated that feeding rats on healthy lettuce leaves significantly caused an increase in HDL-c, whereas 5% infected lettuce leaves significantly reduced HDL-c in blood serum. In addition, feeding rats on 5% or 10% healthy lettuce leaves caused a depression in LDL-c levels when compared to negative control, also, feeding rats on 5% infected lettuce leaves significantly decreased LDL-c and gave the lowest value.

As regards to VLDL-c, feeding rats on healthy lettuce leaves significantly reduced VLDL-c comparing to control negative group, whereas feeding rats on 5% infected leaves significantly increased the VLDL-c in blood serum.

Vázquez et al. (2012) and Komaki et al. (2014) reported that natural antioxidant compounds extracted from plant sources such as lettuce have become a popular trend because of the general awareness of the importance of a healthy diet and limitation on the use of hazardous synthetic antioxidants. Also, Kim et al. (2016) indicated that lettuce a low - calories, low fat and low - sodium salad vegetable and is
rich in fiber, folate and vitamin C as well as essential minerals such as iron. In addition, Yang et al. (2022) reported that lettuce is rich in water 94 - 95% content and low in calories and also an excellent source of vitamins, minerals, and bioactive compounds such as polyphenols, carotenoids and chlorophyll with related health benefits.

Changes of Uric Acid, urea and creatinine level of normal rats fed on diet supplemented with lettuce leaves:

Data tabulated in Table (4) show the changes of Uric acid level of normal rats fed on diet supplemented with lettuce leaves. It is clear to mention that the Uric acid level of control negative group recorded the highest value when comparing with other groups with significant differences. The mean values were 7.12, 4.28, 6.73, 3.99 and 5.25 mg/dl, respectively. Data tabulated in Table (4) show the changes of Urea level of normal rats fed on diet supplemented with lettuce leaves. It is clear to mention that the Urea level of control negative group recorded the highest value when comparing with other groups with significant differences. The mean values were 120.03, 104.40, 85.16, 53.84 and 42.45 mg/dl, respectively. Data given in Table (4) show the changes of creatinine level of normal rats fed on diet supplemented with lettuce leaves. The obtained data indicated that the creatinine level of control negative group recorded the highest value when comparing with other groups. The mean values were 0.98, 0.68, 0.60, 0.54 and 0.63 mg/dl, respectively. There is non significant difference among the groups 2 and 5 while there is significant difference between the groups 1, 3 and 4.

Table (4): Changes of Uric Acid, urea and creatinine level of normal rats fed on diet supplemented with lettuce leaves:

<table>
<thead>
<tr>
<th>Variables</th>
<th>(G1) Negative control</th>
<th>(G2) Healthy lettuce leaves 5%</th>
<th>(G3) Healthy lettuce leaves 10%</th>
<th>(G4) Infected lettuce leaves 5%</th>
<th>(G5) Infected lettuce leaves 10%</th>
<th>L.S.D (P ≤ 0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±SD</td>
<td>7.12 ± 0.1006</td>
<td>4.28 ± 0.285</td>
<td>6.73 ± 0.075</td>
<td>3.99 ± 0.1248</td>
<td>5.25 ± 0.102</td>
<td>0.2856</td>
</tr>
<tr>
<td>UA (mg/dl)</td>
<td>7.12 ± 0.1006</td>
<td>4.28 ± 0.285</td>
<td>6.73 ± 0.075</td>
<td>3.99 ± 0.1248</td>
<td>5.25 ± 0.102</td>
<td></td>
</tr>
</tbody>
</table>
As regards to renal functions, creatinine showed with the highest level in basal diet group, whereas feeding rats on healthy lettuce leaves in both 5% or 10% level caused a reduction in uric acid, urea and creatinine levels in blood serum. However, feeding rats on 5% or 10% infected leaves caused a depression in urea level and the differences were significant as compared to the treatments.

The kidney and liver functions had effected by lettuce leaves in both healthy or infected leaves. These changes are agreement with those of Uddin et al. (2020) and Mitra et al. (2021). They reported that lettuce is an important natural source of phytochemicals. These molecules, which include glycosylated flavonoids, phenolic acids, Carotenoids, Vitamin B group, Ascorbic acid, tecopherols, and sesquiterpene lactones are vital bioactive nutritional components.

**Histopathological Results:**

**Histopathological examination of liver:**

Microscopically, liver of rats from group 1 revealed the normal histological architecture of hepatic lobule (Photos 1 and 2). In contrast, liver of rats from group 2 showed Kupffer cells activation, sinusoidal leukocytosis (Photo 3), focal hepatocellular necrosis associated with inflammatory cells infiltration (Photo 4) and infiltration of portal triad with inflammatory cells (Photo 5). Meanwhile, liver of rats from group 3 described slight Kupffer cells activation (Photos 6 and 7) and slight congestion of central vein (Photo 8). Furthermore, liver of rats from group 4 showed no histopathological alterations (Photo 9) except slight Kupffer cells activation (Photo 10) and slight vacuolation of sporadic hepatocytes (Photo 11) in some sections. Likewise, liver of rats from group 5 revealed apparent normal hepatic lobule (Photo 12).
<table>
<thead>
<tr>
<th>Photo (1): Photomicrograph of liver of rat from group 1 showing the normal histological architecture of hepatic lobule (H &amp; E X 400).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photo (2): Photomicrograph of liver of rat from group 1 showing the normal histological architecture of hepatic lobule (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (3): Photomicrograph of liver of rat from group 2 showing Kupffer cells activation (black arrow) and sinusoidal leukocytosis (red arrow) (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (4): Photomicrograph of liver of rat from group 2 showing focal hepatocellular necrosis associated with inflammatory cells infiltration (arrow) (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (5): Photomicrograph of liver of rat from group 2 showing infiltration of portal triad with inflammatory cells (arrow) (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (6): Photomicrograph of liver of rat from group 3 showing slight Kupffer cells activation (arrow) (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (7): Photomicrograph of liver of rat from group 3 showing slight Kupffer cells activation (arrow) (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (8): Photomicrograph of liver of rat from group 3 showing slight congestion of central vein (arrow) (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (9): Photomicrograph of liver of rat from group 4 showing no histopathological alterations (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (10): Photomicrograph of liver of rat from group 4 showing slight Kupffer cells activation (arrow) (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (11): Photomicrograph of liver of rat from group 4 showing slight vacuolation of sporadic hepatocytes (arrow) (H &amp; E X 400).</td>
</tr>
<tr>
<td>Photo (12): Photomicrograph of liver of rat from group 5 showing apparent normal hepatic lobule (H &amp; E X 400).</td>
</tr>
</tbody>
</table>
References:


Castoldi, R.; Charlo, HCO.; Melo, DM.; Candido, WS.; Vargas, PF.; Dalpian, T. and Braz, LT. (2014): Obtaining resistant lettuce progenies to downy mildew. Hortic Bras. 32:69-73.


Tobar-Tosse, DE.; Candido, WS.; Marin, MV.; Panizi, RC.; Barbosa, JC. and Braz, I.T. (2017): Resistance of green leaf lettuce lines to the *Bremia lactucae* races identified in São Paulo state. Summa Phytopathologica. 43:55–57.


Vázquez, G.; Santos, J.; Freire, M.S.; Antorrena, G. and


