EXAMINING CARICA PAPAYA LEAF EXTRACT’S POTENTIAL FOR TREATING RATS’ HEPATOTOXICITY AND NEPHROTOXICITY CAUSED BY PARACETAMOL.

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ABSTRACT
Carica papaya is an important economic plant that has many nutritional advantages and, remarkable medicinal purposes including treatment of a wide range of illnesses. Thus, the purpose of this study was to determine how well Carica papaya leaf extract mitigates the effects of paracetamol on blood biochemical markers and oxidative damage of rats. Six groups each group consists of six male albino rats, weighing 150 ± 15 g, were created. Group one consisted of a healthy group; Group two consisted of rats given an ethanol papaya extract (100 mg/kg body weight); Group three consisted of rats given an ethanol papaya extract (200 mg/kg body weight). Rats in group four were given paracetamol (2g/kg b.wt). Rats in group five received a pretreatment of Carica papaya extract (100 mg/kg body weight) and a 30-minute paracetamol treatment. Rats in group six received 200 mg/kg body weight of Carica papaya extract as a pretreatment before receiving paracetamol. The experiment continued for two months. The group receiving paracetamol showed a significant increase in blood markers, including urea, creatinine, AST, ALT, and ALP. As a result of these findings, preventing oxidative stress caused by paracetamol was achieved through pretreatment with Carica papaya extract which improved antioxidant enzymes (CAT and SOD). According to these results, paracetamol-induced liver and kidney damage can be prevented by the hepatoprotective and nephroprotective actions of Carica papaya leaf extract, lowering oxidative stress, boosting antioxidant defenses, encouraging liver cell regeneration, and regaining normal liver and kidney function, helps in mitigating liver and kidney damage.

Keywords: Carica papaya, paracetamol, SOD, CAT, oxidative stress.
INTRODUCTION:

Papaya, scientifically referred to as *Carica papaya*, is an indigenous tropical fruit tree species from Central and South America (Da Silva et al., 2007). The potential therapeutic properties of *Carica papaya* leaves have been widely acknowledged and they have been employed in traditional medicine to treat a multitude of afflictions. The medicinal properties of the leaves are attributed to a variety of bioactive compounds, such as flavonoids, phenolic compounds, and alkaloids (Sharma et al., 2022). The leaves of *Carica papaya* have garnered significant interest in scientific investigations owing to their possible therapeutic attributes. Enzymes such as papain and bioactive compounds including flavonoids, alkaloids, and phenolic compounds are abundant in them. The leaves of *Carica papaya* contain these compounds, which are responsible for their antioxidant, anti-inflammatory, immunomodulatory, and hepatoprotective properties (Heena and Sunil, 2019). *Carica papaya* leaf extract has been ascribed its hepatoprotective properties to its capacity to eliminate free radicals, impede lipid peroxidation, strengthen antioxidant defense mechanisms, and modulate inflammatory pathways. Additionally, the presence of papain, an enzyme with proteolytic activity, is believed to aid in liver cell regeneration and tissue repair (Kong et al., 2021). The putative hepatoprotective effects of *Carica papaya* leaf extract in animal models, including rats, have been the subject of numerous studies (Shaban et al., 2021). The hepatoprotective properties of *Carica papaya* leaf extract are ascribed to its anti-inflammatory, regenerative, and antioxidant attributes (Sharma et al., 2022). These attributes aid in mitigating oxidative stress, minimizing inflammation, and facilitating the regeneration of liver cells. Over-the-counter Paracetamol, often known as acetaminophen, is a widely used medication for pain relief and fever reduction (Ayoub, 2021). It is generally considered safe when used within the recommended dosage. However, excessive or prolonged use of paracetamol can lead to hepatotoxicity, primarily due to the production of toxic metabolites through the cytochrome P450 pathway (Offor et al., 2022). However, it can cause hepatotoxicity, which is characterized by liver damage and dysfunction at high doses or with prolonged use (Rotundo and Pyrsopoulos, 2020). Rats are commonly used as animal models to study paracetamol-induced hepatotoxicity due to their physiological and genetic similarities to humans (Xu et al., 2021). These studies have demonstrated promising results, suggesting that *Carica papaya* leaf extract possesses hepatoprotective properties that may help mitigate paracetamol-induced liver damage.

MATERIALS AND METHODS:

Source of *Carica papaya* leaves

*Carica Papaya* leaves were obtained from a farm. The faculty of agriculture at Minia University Abdou, M.A.H. Professor of Ornamental Plants, Horticulture Department, Faculty of Agriculture, Minia University, Egypt who identified the plant. For extraction, the leaves were washed, dried naturally,
and subsequently powdered into a fine powder.

**Chemicals:**

Assay tablets of paracetamol were purchased from a local pharmacy in Minia city. From Bio Diagnostic Chemical Company, kits were obtained to measure serum protein, albumin, AST, ALT, urea, creatinine, uric acid, glutathione reduced, catalase, and SOD. All other solvents and chemicals utilized were of the highest quality available in the market.

**Preparation of plant extract:**

Molecular target compounds were isolated from papaya leaves utilizing a combination of polar and non-polar solvents, including ethyl acetate, acetone, and ethanol. The ethanol, acetone, and ethyl acetate extracts of *Carica papaya* leaves were prepared with minor modifications to the method described by Abdullah *et al.* (2014).

**Estimation of total phenolic and flavonoid contents:**

The determination of total flavonoid content (TFC) and total phenolic content (TPC) was conducted utilizing colorimetric and Folin-Ciocalteu photometric assays, respectively (Yoo *et al*., 2008).

**Experimental animals and Design:**

The Sprague-Dawley strain albino rats, consisting of 36 males and weighing approximately 150 ± 15 g each, were obtained from Nahda University and housed in the Biological Laboratory of the Department of Biological Chemistry at Minia University's Faculty of Agriculture. Every experiment was conducted in adherence to the protocols established by the Agriculture Chemistry department of the Faculty of Agriculture in Minia, Egypt, in accordance with the guidelines for animal research provided by the Ethics Committee Approval No. (MU/FA 022/12/22). The research was carried out in adherence to the regulations set forth by the institution and local legislation. Rats were housed in plastic cages within a chamber with 25 ± 2 air conditioning (alternating light and dark periods every 12 hours). A two-week supply of commercially balanced meals and unrestricted potable water were provided prior to the commencement of the trial. Weight was recorded for each rodent at the beginning of the experiment and then weekly until its conclusion. In order to evaluate the effects of *carica papaya* leaf extract on normal rats, six groups of six rodents each were established after the acclimation phase.

**Treatment was started then continued for two month as follow.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>Control</td>
</tr>
<tr>
<td>Group (2)</td>
<td>C.P (100 mg/kg b.w) the extract was suspended in 2ml of 2% w/v carboxy methyl cellulose (walia <em>et al</em>., 2011).for 60 days</td>
</tr>
<tr>
<td>Group (3)</td>
<td>C.P (200 mg/kg b.w) the extract was suspended in 2ml of 2% w/v carboxy methyl cellulose (walia <em>et al</em>., 2011).for 60 days.</td>
</tr>
<tr>
<td>Group (4)</td>
<td>Paracetamol (2g/kg b.w daily) given orally by stomach according to Senthilkumar <em>et al</em>., (2014).</td>
</tr>
<tr>
<td>Group (5)</td>
<td>C.P (100 mg/kg b.w) in the same of group 2+ Paracetamol (2g/kg b.w daily).</td>
</tr>
<tr>
<td>Group (6)</td>
<td>C.P (200 mg/kg b.w) in the same of group 3+ Paracetamol (2g/kg b.w daily).</td>
</tr>
</tbody>
</table>
Rats were given an overnight fast and then anesthesia to obtain blood samples from the retro-orbital plexus at the conclusion of the 60-day period (Schermer 1967). After allowing the blood to coagulate at room temperature, it was centrifuged for 15 minutes at 40 °C at 3000 rpm. For use in various biochemical parameters, including serum protein (Gornall et al., 1949), albumin (Dumas et al., 1971), urea (Fawcett and Scot, 1960), creatinine (Murray, 1984), uric acid (Barham and Tinder, 1972), glutathione reduced (Beutler et al. 1963), catalase (Aebi, 1984), and SOD (Nishikimi et al., 1972).

**Histopathological Examinations:**

Autopsy samples from rats in various groups' livers and kidney were obtained, and the slides made according to Bancroft et al., (1996).

**Statistical analysis:**

Utilizing the means and standard deviations of six parallel measurements, the experimental data were statistically analyzed. Methods of analysis of variance (ANOVA) were implemented. To perform the statistical computations, the GraphPad Prism® software (GraphPad Software, San Diego, CA, USA) was utilized (Motulsky, 1999).

**RESULTS AND DISCUSSION:**

**Quantitative screening of phytochemicals:**

The total phenolic contents of the *carica papaya* extract are displayed in Table (1), where the highest values, approximately 33.75 and 30.50 mg/m total phenolic contents, are found in the ethanol and acetone extracts. Ethyl acetate extract, on the other hand, showed a value of 28.83 mg/m. The acetone extract has the highest flavonoid content in the same table, with values of around 28.75 and 25.75 mg/m, followed by the ethyl acetate extract at 25.00 mg/m. Plant phenolic extracts consist of various kinds of phenols that are soluble in various solvents. According to Zohra (2011), alcohol yields positive results for the extraction procedure. The most effective solvent for removing polyphenols from *carica papaya* leaves is alcohol solutions (Victor et al., 2018). According to Omidiwura (2018), the yield of phenols produced by ethanol solvent was higher than that of other solvents while remaining constant.

<table>
<thead>
<tr>
<th>Extracts</th>
<th>Total phenolic compounds (mg/g)a</th>
<th>Total flavonoids (mg/g)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol extract</td>
<td>33.75± 4.6</td>
<td>25.00± 3.30</td>
</tr>
<tr>
<td>Acetone extract</td>
<td>30.50± 3.5</td>
<td>28.75± 0.90</td>
</tr>
<tr>
<td>Ethyl acetate extract</td>
<td>28.83± 4.21</td>
<td>25.75± 1.00</td>
</tr>
</tbody>
</table>

*a: milligrams of gallic acid equivalent per gram of dry leaf extract; b: milligrams of quercetin equivalent per gram of dry leaf extract. Each number is represented as the mean plus or minus the standard deviation, with a sample size of 6.*
Body Weight Gain and daily feed intake in Tested Animals:

Changes in body weight increase and daily feed consumption in animals subjected to testing are displayed in Table 2. After two months of paracetamol treatment, rats' daily feed intake and body weight increase were marginally lower than those of the normal control group. While daily feed intake and body weight growth were still lower than normal control, the treatment groups, which received Carica papaya at two doses (100 mg, 200 mg) in addition to paracetamol exhibited an increase in these areas when compared to paracetamol alone.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean Final body weight (g)</th>
<th>Mean Body weight gain (g)</th>
<th>Daily feed intake (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>327±13.6</td>
<td>171±8.2</td>
<td>18</td>
</tr>
<tr>
<td>Cp1</td>
<td>280±29.1</td>
<td>118.3±2.5</td>
<td>20.6</td>
</tr>
<tr>
<td>Cp2</td>
<td>285±14</td>
<td>136.3±1.1</td>
<td>20.2</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>224±24.4*</td>
<td>56±28.6*</td>
<td>12.91</td>
</tr>
<tr>
<td>Cp1 paracetamol</td>
<td>248±37a</td>
<td>86±26.9ab</td>
<td>17.43</td>
</tr>
<tr>
<td>Cp2 paracetamol</td>
<td>228±13.5*</td>
<td>74.33±8.1bd</td>
<td>15.91</td>
</tr>
</tbody>
</table>

The mean ± standard deviation of observations was calculated for six rodents. *Notably distinct from the control group (P < 0.05); bNotably distinct from the group administered paracetamol (P < 0.05). CP1 and CP2 contain 100 and 200 mg/kg b. wt., respectively, of carica papyra extract.

Impact of paracetamol and carica papaya extract (100, 200 mg/kg b. wt.) on a few biochemical parameters in the serum of test rats.

Liver functions:

Serum variations in AST, ALT, ALP, and total protein albumin are displayed in (Table 3). Rats given paracetamol for two months had lower blood levels of albumin and total protein than the normal control group. In contrast, the treated groups that received Carica papaya at two doses (100 mg and 200 mg) in addition to paracetamol showed an increase in total protein and albumin, though these values were still lower than those of the normal control group. Serum ALT, AST, and ALP activity were also decreased. Sensitive indicators for evaluating liver injury included serum ALT and AST activity (Li et al., 2018). It’s also important to remember that the enzyme alkaline phosphatase (ALP), being found in both the liver and the bones, is essential for the removal of phosphate groups. The present results are consistent with those of El Menyiy et al. (2018) and Naggayi et al. (2015), who found that, paracetamol significantly, decreased serum total protein and albumin and elevated aspartate and alanine aminotransferase activities when compared with the control. Additionally, Koshak et al. (2023) found that administering a sub-lethal dosage of paracetamol (2 g/kg) resulted in liver damage in the rats, as evidenced by a marked rise in the blood levels of alkaline phosphatase (ALP) and transaminases (AST and ALT).
Table 3. Effects of C.P1 and C.P2 on Liver function in Serum of Albino Rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total Protein(g/dl)</th>
<th>Albumin(g/dl)</th>
<th>AST(u/ml)</th>
<th>ALT(u/ml)</th>
<th>ALP(u/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5.34±0.057</td>
<td>2.867±0.5774</td>
<td>38.30±1.10</td>
<td>31.10±1.73</td>
<td>2.77±0.251</td>
</tr>
<tr>
<td>Cp1</td>
<td>4.24±0.208*a</td>
<td>2.18±0.05*a</td>
<td>42.30±1.61</td>
<td>41.47±1.78</td>
<td>9.33±0.153</td>
</tr>
<tr>
<td>Cp2</td>
<td>4.74±0.10</td>
<td>2.533±0.05</td>
<td>49.40±0.76</td>
<td>37.27±3.47</td>
<td>7.17±0.838</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>1.74±0.10*a</td>
<td>1.17±0.15*a</td>
<td>111.5±1.57</td>
<td>82.90±5.23</td>
<td>22.60±1.05*a</td>
</tr>
<tr>
<td>Cp1+paracetamol</td>
<td>2.94±0.10*ab</td>
<td>1.40±0.10*ab</td>
<td>86.65±3.85</td>
<td>59.23±4.33</td>
<td>21.00±0.700*</td>
</tr>
<tr>
<td>Cp2+ paracetamol</td>
<td>3.94±0.458*ab</td>
<td>2.07±0.1528*ab</td>
<td>78.77±3.29</td>
<td>46.40±3.20</td>
<td>15.23±1.71*ab</td>
</tr>
</tbody>
</table>

The mean ± standard deviation of observations was calculated for six rodents. *Notably distinct from the control group (P < 0.05); †Notably distinct from the group administered paracetamol (P < 0.05). Cp1 and Cp2 contain 100 and 200 mg/kg b. wt., respectively, of carica papaya extract.

Rats' liver enzyme levels rose when given paracetamol. Increased hepatic dysfunction or pathology, such as blocked bile ducts or particular skeletal deformities, may be indicated by elevated alkaline phosphatase values. Depleted glutathione, high reactive oxygen species, and cytochrome P450 isoforms were recognized to contribute to the pathophysiology of paracetamol-induced liver injury. It's interesting to note that *carica papaya* extract inhibited different isoforms of cytochrome 450. This suggests that inhibition of cytochrome P450, reduces the formation of N-acetyl-p-benzoquinone imines and maintains the glutathione pathway active. Subsequently, *carica papaya* extract may mitigate the negative effects of paracetamol toxicity. The results of other research (Ojo et al., 2006; Jiang et al., 2017) are consistent with the elevation of liver enzymes caused by high dose of paracetamol. Since the liver is where albumin is mostly generated, a fall in serum albumin and total protein caused by an overdose of paracetamol is another sign of liver damage. Proteinuria brought on by a large dose of paracetamol may be the cause of this effect on serum albumin and total protein (Sugimoto et al., 2011).

**Kidney function:**

Changes in serum renal function levels are displayed in (Table 4). Rats given paracetamol for two months had higher serum levels of urea and, creatinine while uric acid was lower than the normal control group. In another hand the treated groups with *Carica papaya* at two doses (100 mg, 200 mg) in combination with paracetamol showed decrease of urea, creatiion and increase uric acid compared to paracetamol alone . The present result are in the same line as those by El Menyiy et al.(2018) and Naggayi et al. (2015) who found that paracetamol considerably raised blood creatinine and blood urea nitrogen, but it dramatically decreased serum uric acid.
Table 4. Effects of C.P1 and C.P2 on kidney function Level m(g/dl) in Serum of Albino Rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Uric acid (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>9.60±1.015</td>
<td>0.66±0.577</td>
<td>5.20 ±0.346</td>
</tr>
<tr>
<td>Cp1</td>
<td>10.33±0.152</td>
<td>0.86±0.577</td>
<td>4.20 ±0.6</td>
</tr>
<tr>
<td>Cp2</td>
<td>11.50±0.200</td>
<td>1.00±0.100</td>
<td>4.43 ±1.21</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>13.73±1.29</td>
<td>3.13±0.057</td>
<td>2.50 ±0.200</td>
</tr>
<tr>
<td>Cp1 paracetamol</td>
<td>11.87±2.76</td>
<td>1.40 ±0.100</td>
<td>3.20±0.100</td>
</tr>
<tr>
<td>Cp2 paracetamol</td>
<td>11.7±1.484</td>
<td>1.13 ±0.208</td>
<td>3.56 ±0.550</td>
</tr>
</tbody>
</table>

The mean ± standard deviation of observations was calculated for six rodents. 

Additionally, Hegazy et al.’s study in 2021 found that administering paracetamol to the group receiving treatment caused a discernible decline in the biochemical alterations found in that group. Prolonged increases in serum urea and creatinine concentrations were observed in response to the biological modifications. The results are consistent with those of Jaz et al. (2016), who discovered that the administration of paracetamol significantly increased serum concentrations of urea and creatinine (P < 0.05), when comparison to the control group.

Oxidative Enzymes

Table (5) displays the hepatic and renal GSH, CAT, and SOD activity. Changes in the blood levels of SOD, GSH, and catalase for the kidney and liver are displayed in Table 9. Rats given paracetamol for two months had lower serum levels of SOD, GSH, and catalase for the kidney and liver than the normal control group. While SOD, GSH, and catalase levels in the kidney and liver were higher in the treated groups given *carica papaya* at two doses (100 mg, 200 mg) in addition to paracetamol than the corresponding levels on giving the paracetamol alone. Both treatments were remained lower than in the normal control group.
Table 5. Effects of carica papaya leaves extract at two doses and paracetamol on hepatic and renal SOD, GSH and CAT in rats of Albino Rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>SOD Liver (U/ml)</th>
<th>SOD Kidney (U/ml)</th>
<th>Catalase Liver (U/g protein)</th>
<th>Catalase Kidney (U/g protein)</th>
<th>GSH Liver (mg/g)</th>
<th>GSH Kidney (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>355.7 ± 4.7</td>
<td>368.3±6.3</td>
<td>165±1.73α</td>
<td>81.7±4.04</td>
<td>3.30±0.100</td>
<td>4.26±0.321</td>
</tr>
<tr>
<td>Cp1</td>
<td>330.3±3.5</td>
<td>344 ± 6.3</td>
<td>163±5.00</td>
<td>100±0.577</td>
<td>2.80±0.100α</td>
<td>3.30±0.173α</td>
</tr>
<tr>
<td>Cp2</td>
<td>336 ±3.65</td>
<td>364.7 ± 8.3</td>
<td>164±1.15</td>
<td>115±3.22</td>
<td>2.83±0.115α</td>
<td>3.50±0.360α</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>164 ± 8.00c</td>
<td>114.3 ±3.5c</td>
<td>84±2.98c</td>
<td>203.3±1.53c</td>
<td>1.46±0.159c</td>
<td>1.33±0.321c</td>
</tr>
<tr>
<td>Cp1 + paracetamol</td>
<td>222±3.7.0b</td>
<td>242.3 ± 4.8ab</td>
<td>87.33±3.05a</td>
<td>145±7.57ab</td>
<td>1.60±0.115a</td>
<td>2.26±0.115ab</td>
</tr>
<tr>
<td>Cp2 + paracetamol</td>
<td>283.3±54.12ab</td>
<td>276 ± 5.6ab</td>
<td>149±2.51ab</td>
<td>129±3.00ab</td>
<td>2.30±0.057ab</td>
<td>2.13±0.321ab</td>
</tr>
</tbody>
</table>

The mean ± standard deviation of observations was calculated for six rodents. α Notably distinct from the control group (P < 0.05); b Notably distinct from the group administered paracetamol (P < 0.05). Cp1 and Cp2 contain 100 and 200 mg/kg b. wt., respectively, of carica papaya extract.

Enzymatic antioxidants are essential because they shield cells from oxidative damage. The present findings are consistent with those of Kandemir et al. (2017) and, Aboshama et al. (2024), Whose found that paracetamol dramatically decreased the antioxidant activity of SOD and CAT in the liver renal tissue when compared to the control group. Additionally, Okokon et al. (2017) demonstrated that paracetamol administration resulted in significant decreases in the activities of SOD, catalase, and GSH level in liver tissue when compared with the control group. Conversely, Raffaelli et al. (2015) assessed the antioxidative potential of goods made from C. papaya yeast fermentation. Subsequently SOD activity significantly increased. Sadek (2012) looked into how C. papaya extracts shielded rats' liver and kidney enzymes from acrylamide-induced damage.

Histopathological examination of liver:

The livers of rats in the control group exhibited normal histoarchitecture of hepatic tissue when observed microscopically (Fig 1. a). Furthermore, liver of rats from groups given carica papaya extract (100, 200mg /kg) exhibited no histopathological lesions (Fig 1. b, c). On contrary, liver of rats from group paracetamol described necrosis of sporadic hepatocytes (Fig 1. d), ballooning degeneration of
hepatocytes congestion of hepato portal blood vessel vacuolar degeneration of hepatocytes and focal hepatocellular necrosis. Meanwhile, liver from group given *carica papaya* extract (100mg) with paracetamol revealed Kupffer cells activation (Fig 1. e), slight hydropic degeneration of hepatocytes and congestion Furthermore, sections from group given *carica papaya* extract (200mg) with paracetamol exhibited only slight hydropic degeneration of hepatocytes (Fig 1. f).

**Fig 1. Histopathological examination of liver:** (a): Photomicrograph of liver of rat from group control showing the normal histoarchitecture of hepatic tissue (H & E X 400, scale bar 25μm). (b): Photomicrograph of liver of rat from group c.p1 showing no histopathological lesions (H & E X 400, scale bar 25μm). (c): Photomicrograph of liver of rat from group carica papaya (200mg kg⁻¹) showing no histopathological lesions (H & E X 400, scale bar 25μm). (d): Photomicrograph of liver of rat from group paracetamol showing necrosis of sporadic hepatocytes (red arrow) and ballooning degeneration of hepatocytes (black arrow) (H & E X 400, scale bar 25μm). (e): Photomicrograph of liver of rat from group c.p1 + para showing Kupffer cells activation (black arrow) (H & E X 400, scale bar 25μm). (f): Photomicrograph of liver of rat from group c.p2+ para showing slight hydropic degeneration of hepatocytes (arrow) (H & E X 400, scale bar 25μm).
The results of our study align with the observations made by Okokon et al. (2017), which indicated that rodents administered paracetamol exhibited a disorderly appearance of healthy hepatic cells, hyperplasia, centrilobular necrosis, vascular and cellular degeneration, polymorphonuclear aggregation, inflammation, and fatty degeneration.

Histopathological analysis of the kidneys:

The kidneys of rats from groups Cp1, Cp2, and control exhibited a normal histological structure of renal parenchyma when viewed microscopically. (Fig 2.a, b, c). In addition, renal tubule epithelial lining vacuolar degeneration was observed in the kidneys of rats in the paracetamol group (Fig 2.d). Conversely, glomerular tuft congestion was marginal in sections from the Cp1 para group (Fig 2.e). Nevertheless, certain sections from group Cp2 para did not exhibit any discernible histopathological changes (Fig 2.f). These findings are consistent with those of Hegazy et al. (2021), who demonstrated that paracetamol induced distinct histopathological alterations in the medulla and renal cortex. The results of Ahmed et al. (2015) indicate that a high dose of paracetamol can lead to an increase in permeability of renal blood vessels. This, in turn, can cause interstitial edema and severe congestion in the glomerular tufts and renal blood capillaries. These findings align with the observed hypertrophy, hypercellularity, and congestion of glomerular capillaries in the current study. Moreover, hypercellular glomeruli are present in the renal cortex as a consequence of the mesangial cells’ enhanced proliferation (Aziz et al., 2013).
Figure 2. Histopathological examination of kidneys (a): Group control showing the normal histological structure of renal parenchyma (H & E X 400, scale bar 25μm). (b): Group c.p1 showing the normal histological structure of renal parenchyma (H & E X 400, scale bar 25μm). (c): Group c.p2 showing the normal histological structure of renal parenchyma (H & E X 400, scale bar 25μm). (d): Group para showing marked vacuolar degeneration of epithelial lining renal tubules (black arrow) and congestion of intertubular renal blood vessel (red arrow) (H & E X 400, scale bar 25μm). (e): Group c.p1 para showing slight congestion of glomerular tuft (arrow) (H & E X 400, scale bar 25μm). (f): Group c.p2 para showing no histopathological alterations (H & E X 400, scale bar 25μm).
Conversely, a subset of the renal glomeruli examined in this investigation exhibited glomerular atrophy. The observed phenomena can be explained by a reduction in the glomerular filtration of the drug due to capillary constriction. Renal tubules exhibited tubular dilatation, necrosis of tubular cells, sloughing of necrotic tubular epithelial cells into the lumens of tubules, substantial cytoplasmic vacuolization, tubular cell enlargement, and darkly stained nuclei. In accordance with the findings documented by Kirbas et al. (2015), substantial deformation was observed in the epithelial cell structures of both the proximal and distal tubules. Cellular shedding of the epithelium of the distal tubules was induced by lumen dilatation and edematous fluid, whereas the proximal tubules’ distended epithelial cells caused extensive degeneration of structures.

**CONCLUSION:**
According to the present study's findings, oxidative damage and blood biochemical indicators can be lessened by paracetamol when given in doses of 200 mg / kg of *carica papaya* extract. The efficacy of *carica papaya* extract in reducing the toxicity of paracetamol may be attributed to its antioxidant characteristics.
REFERENCES:


دراسة قدرة مستخلص أوراق الباباظ لعلاج التسمم الكبدي والكلي لدى الجرذان الناجم عن الباراسيتامول.

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يعتبر الباباظ من النباتات الاقتصادية الهامة التي لها فوائد غذائية كثيرة، وأغراض طبية رائعة، وتستخدم لإنتاج المواد المستخدمة في علاج مجموعة واسعة من الأمراض. وإذا كانت هذه الدراسة تحديد مدى نجاح مستخلص أوراق الباباظ في تخفيف آثار الباراسيتامول على العلامات البيوكيميائية في الدم والأضرار التأكسدية فيما يتعلق بالجرذان أجريت التجارب في قسم الكيمياء الزراعية - كلية الزراعة – جامعة المنيا. في القسم تم تقسيم ذكور الجرذان إلى ست مجموعات كل مجموعة مكونة من ستة فئران ألبينا، وزنها 150 ± 15 جم. المجموعة الأولى تتكون من مجموعة صحية؛ تتألف المجموعة الثانية من فئران أعطت مستخلص الباباظ الإيثانول (100 ملجم/كجم من وزن الجسم)، أعطت الفئران في المجموعة الرابعة الباراسيتامول (2 جرام/كجم من وزن الجسم). نُقِّى الفئران في المجموعة الخامسة معالجتهم بمستخلص الباباظ (100 ملجم/كجم من وزن الجسم) مع الباراسيتامول، نقلت الفئران في المجموعة السادسة معالجتهم بمستخلص الباباظ 200 ملجم/كجم من الجسم مع الباراسيتامول. تم انتهاء التجربة بعد شهرين، حيث أظهرت المجموعة التي تناولت الباراسيتامول زيادة محذوفة في المؤشرات الحيوية، بما في ذلك البوريا والكرياتينين وALT وAST. نتيجة لهذه النتائج، تم تحقيق منع الإجهاد التأكسدي الناجم عن الباراسيتامول من خلال معالجتهم السبعة مستخلص الباباظ الذي يحسن الإزمنات مضادة للرطوبة (CAT) و (SOD). ويعتبر الباباظ من فئات الكبد والكلى الناجم عن الباراسيتامول بالاستخدام مستخلص أوراق الباراسيتامول من خلال خفض الإجهاد التأكسدي، وتعزيز الدفاعات مضادة للأكسدة، وتشجيع تجديد خلايا الكبد، واستعادة وظائف الكبد والكلى الطبيعية، وكذلك المساعدة على تخفيف تلف الكبد والكلي.