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# Citric Acid in Dairy Products Alters Liver and Kidney in Mice

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**Abstract.** General Background: Food preservatives like citric acid are widely used in dairy products to inhibit microbial growth and extend shelf life. Specific Background: Although generally recognized as safe, concerns have arisen regarding potential adverse health effects with long-term or high-dose consumption. Knowledge Gap: Limited research exists on the histopathological and biochemical effects of citric acid as a preservative in mammalian models. Aims: This study aimed to assess the impact of oral administration of citric acid (3%) on liver and kidney tissues, as well as on biochemical markers in male white mice. Results: Histological analyses revealed notable degenerative changes in liver and kidney tissues, including glomerular shrinkage, inflammatory infiltration, hepatocyte vacuolization, and sinusoidal hemorrhage. Biochemically, treated mice exhibited significant elevations in ALT, AST, serum creatinine, and urea levels compared to controls ($p < 0.05$). Novelty: This study provides integrated evidence from both histological and biochemical parameters demonstrating the potential toxicity of citric acid when used excessively. Implications: Findings suggest the need for reevaluation of citric acid's safety profile at common exposure levels and encourage further toxicological studies to inform food safety standards.

**Keywords:** Citric Acid, Dairy Products, Kidney, Liver, Preservatives

## I. INTRODUCTION

Food is an necessary thing for human survival that is composed of a wide range of chemicals other than the macro and micro nutrients directly required to support life [1]. The human diet therefore contains a variety of chemicals, both naturally present and those intentionally added to food. One of these substances are antioxidants which are used as food preservatives (Food additives) [2].

Food additives can be defined by the Food and Drug Administration (FDA) as any substances which not normally consumed as the food itself' which are added to food to do a technological purpose such as to improve appearance (Colouring), taste (Flavouring) and keeping good food qualities (antioxidant, preservation) [3]. So the food preservation are employed to ensure safety and avoid quality loss derived from microbial, physical–chemical, or enzymatic reactions . It used to preserve a food, to keep it from spoiling for a period longer than it would have kept fresh ,and to maintain the quality, texture, consistency, taste, color, alkalinity or acidity by prevent the food spoilage [4][5]. Food spoilage is a worldwide problem where the food detail will lose its texture, quality, flavor, and it will be no more appropriate for consumption [6][7]. Dairy products such as cheese, milk and yoghurt [8][9]

These dairy products consist of numerous nutrient content (like protein, minerals and vitamins), it serves as an excellent . Thus, food products is that they decline over a short period of time so different food preservation are used to eliminate the growth of spoilage-causing microorganisms and maintaining the nutritional properties of milk[10][11][12] to improve their freshness, safety, texture, taste , and to prevent the food spoilage, food additives are being added during processing that consider an important step to limit the growth of organisms in milk products [13][14]. The preservative acted by disrupting cell membranes of moulds and, yeasts affecting leakage and last lysis[15], preservative inhibition the growth by the number of activities including accumulation of toxic anions, inhibition of essential metabolic reaction, and stress on intracellular pH homeostasis [16]. Though preservatives play an important role in food safety, many studies have shown that may affect organisms that consume them harmfully.

Free radicals formed during the detoxifying oxidation/reduction reactions of food additives cause damage of tissues [17].

Although some of these substances are harmless when used in small amount, the use of others is hazard to human health [18][19]. Studies note it is safe to eat foods contain preservatives within ADI (Acceptably daily intake ) [20]. When people eat foods containing these preservatives in large amounts, they can experience toxic effects [21][22]. Recent toxicological studies indicate that certain concentrations of preservatives and their continuous use may be potentially mutagenic and genotoxic when used for a long time [23][24]. Preservatives must meet standards for their use, similarly to other classes of food additives, they are chemicals and may cause opposite health effects. The excessive intake of these preservatives might be potentially dangerous to the consumers [25]. Current toxicological studies show that the concentrations of preservatives and their continuous use may be potentially as cancer causing or agents carcinogens [26]. The side effects of preservatives are breathing difficulty, skin rashes and itching, sneezing or gastrointestinal upsets can be create [18]

There are many type of preservatives, but the major type are nisin, sodium benzoate[27] and citric acid that used as a natural preservative [28] which is used for avoiding antimicrobial growing in processed foods, also has an antioxidant effect is used in many ready foods, particularly in cheese is known to have a flavor enhancer effect [29]

The symbol (E330) referred to citric acid that write in the cover of dairy products [30]. In the European Union, an E number refers to all food additives. The E-number expression that used in the food ingredient label while "E" is for European safety agreement. The agreement of a substrate as a food additive is intended to both confirm the protection of public health regarding the use of a food additive and number to inform consumers about the presence of name of food additive that found in food products [31].

Citric acid is an organic acid originate in the greatest amounts in citrus fruits [32][33]. Citric acid is the greatest common type of food additives, acidity regular [34] and an antioxidant [35]. Citric acid is used as pH control agent, preservatives to prevent microbial growth, also used as a flavoring agent and preservative in food, especially in biscuit, prepared soup, cake, cheese and cheese products, baby food, chewing gum, margarine, fizzy lemonade, fish, meat, and beverages, especially soft drinks [28]. However they were reported to have carcinogenetic effects when used in high doses [36].

The study on effect of citric acid on the kidney of mice noted tubules demonstration desquamated cells, shrinkage of glomeruli, Bowman’s spaces were lobulated and contracted tufts [37]. The primary cause of histopathology changes in renal structure when citric acid covalent attachment to bioactive protein lead to changes in membrane permeability and related enzyme activities [28].

The effects of citric acid treated to rats noted desquamation or moderate dilatation of kidney tubules distinct renal capsule spaces, and lobulated tufts [17]. Also in the study of oral administration of citric acids to a rate noted significant increase in the level of serum creatinine and in the level of serum urea nitrogen . Also showed causes damage to renal function [37].

The studies noted the effect of citric acid on to the liver mice caused picnotic nuclei, loosing and combining of hepatocyte membranes, cell infiltration in small areas in liver can be expressed as a protective response that happened in contradiction of the degenerative effects of citric acid. Also cytoplasmic vacuolization in hepatocytes, damage of blood vessel endothelium in the liver. In the study of oral administration of citric acids showed increased of ALT and AST enzyme [38].

## II. MATERIALS AND METHODS

### A. Experimental Animals

Forty matured male white mice with weighing range 27-30gm, each were used for the experiments were bought from Drug and Healthy center in Baghdad, Iraq. Mice were preserved in plastic cages, all these cages put in the animal house under temperature 24±1°C and humidity situation (65%) with feeding by using standard pellets for about 14 days to acclimatize before the experiment.

**B. Chemical and Exposure Dose**

The useful citric acid concentrations in drinking water were chosen based on the recent ecological study agreed by the present authors [39], the dose level of citric acid was measured as following: Dilution 3 g of citric acid in 100 ml of distal water for get diluted citric acid 3% then 1 ml orally administered for a period of 30 days give for each mouse.

**C. Experimental Design**

Forty mice ( male ) were divided into two main groups; as a control and treatment group.

1. Control group: there were 10 mice were orally administered with distilled water
2. Treatment groups: There were 30 mice which administered by citric acid that daily dissolved in distilled water for 30 days. All mice were sacrificed at the end of 30 days.

**D. Preparation of Histological and Biochemical Studies**

After the end of the treatment period, the mice were anesthetized using chloroform and sacrificed by bleeding from common carotid artery and the blood samples were collected into clean and dry centrifuge tubes, then centrifuged for at ( 3000 rpm ) for 15 minutes and non-hemolysis serum was separated for biochemical analysis (the level of serum creatinine and the level of serum urea). Liver and kidney were dissected out carefully from the mice using standard procedure. Collected organs were washed with normal saline then organs were cut into small tissue pieces by using a surgical scalpel for allowing easy penetration of the chemicals inside the tissue to easily light microscopic study.

1) Fixation: the tissue sections were preserved in 10% formalin solution for a period of 48 hour
2) washing under running tap water for one hour until complete removal of most of the formalin from the tissues. dehydration of the tissues was conducted by immersing the tissue in a series of gradually increasing concentrations of alcohol (50%, 70%, 80%, 90%, and absolute alcohol).
3) Clearing it is obligatory because the used alcohol for dehydration will not dissolve or mix with molten paraffin. Blocking means the samples embedded into paraffin wax for making blocks. The block was to be cut by removing of wax from the surface of the block to expose the tissue
4) Cutting of the tissue was performed by using a microtome. The microtome was preset to cut the tissue as thicknesses with 5 µm. Blocks Small ribbons of tissue sections were placed on a microscopic slide with help of warm distil water containing few drops of Mayer's albumen with xylene solution, the slide was put on the hot plate with (40°c) for overnight.
5) Staininghaematoxylene and eosin yellow solution were used to stain the tissue for preparing permanent slide. Histopathological changes were observed under a light microscope and snaps were taken.

**E. Statistical Analysis**

The data obtained was statistically assessed by using SPSS program to assess the significance of changes between the control and treated mice group results. We used the one sample t-testto test the hypothesis of the study. The results were expressed as Means with a p. value equals 0.05 as statistical significance..

## III. RESULTS AND DISCUSSION

**A. The Histological Results and Discussion**

**1. Effect of Citric Acid on Kidney**

In our study, the result of the kidney in mice after oral administration with 1 ml of citric acid noted significantly increase in the diameter of the renal corpuscle which become (24.45±0.48µm) in the treated group when compared with control group (Tab. 1). This result denoted to acute progressive in the renal corpuscle after treated with citric acid which leads to shrinkage of the renal corpuscle. This histological change in the renal corpuscle may be due to the toxicity of citric acid on the renal corpuscle.

The tissue section of the cortical region in the kidney showed aggregation of inflammatory cells, blood congestion and wide abnormal cystic dilution filled with blood. Also, the result noted the renal corpuscle has wide Bowman's space and shrinkage of glomeruli (Fig. 1,2). These histological changes of kidney after treated with citric acid were similar to Chen et al., [17] which noted the kidney of the mice when treated with citric acid caused shrinkage of glomeruli, wider renal capsule spaces and severe dilation of renal tubules and some tubule lumens were irregular.

The results noted that the wall of P.C.T. has no high significantly increase in diameter with (10.08±0.19µm) compared with a control group (Tab. 1). The histological section noted acute degeneration in the wall of P.C.T and exfoliated the epithelia to the lumen of P.C.T.(Fig. 3) . The tissue section of the D.C.T showed increased in diameter (16.82±0.24) compared with a control group . Also, the result noted severe damage in the wall of D.C.T and exfoliated of epithelial layer due to toxicity of these food preservatives (Fig. 4).

In the tissue section of descending limp of the Henley loop have wide diameter (10.171±0.13µm) while ascending Henley loop have no significant increase in diameter (12.59±0.17µm), both branches ascending and descending arms of the Henley loop characterized by have acute lumen with very prominent basement membrane in the wall of the Henley loop (Tab. 1). Mostly have acute degeneration in the wall and exfoliated the epithelia into the lumen (Fig. 5). The same finding was recorded by Aktac, et al. which noted the kidney of mice when treated with citric acid caused degenerations of tubules and fusing of tubules may due to materials toxicity of citric acid metabolism.

**2. Effect of Citric Acid on Liver**

The tissue section of liver after 30 days of treated oral administration with 1ml citric acid noted that slightly significance increased in the thickness of the capsule (6.25±0.20µm) and the diameter of hepatocyte nuclei (8.793±0.12µm) when compared with the control group (Tab. 1).These results referred as the treated with citric acid have slight effects on the liver capsule of the treated group.

The histological result of the liver showed the liver parenchyma has prominent degeneration, damage in hepatic cords and large spaces were detected in some areas due to the degeneration of hepatocytes (Fig. 6). This result may be due to the lysosome action, that are very sensitive to any pathologic influence, are ruptured and then released their powerful enzymes, which cause degeneration of different cellular compounds. This histological change of liver after treated with citric acid were agreement with Aktaç et al., [38] which noted the liver of mice when treated with citric acid have necrotic lesions. These changes were degeneration of tissue, cytoplasmic vacuolization, damage in hepatic cords and hemorrhage.

The tissue section of the liver showed damage in hepatic cords with dilation in the sinusoids with hemorrhage (Fig. 7). This histological change of liver after treated with citric acid was constant with Abushofa et al., which noted the liver sections after treated with preservatives showed enlargement of blood sinusoids appear between hepatocytes with damage appeared as a vacuoles in the cytoplasm.

The current result in the liver of the treated group with citric acid appeared enlargement or hypertrophy of hepatocytes in small segments of destruction hepatic cords. The tissue figures showed wide space a rounded the central vein some of its filled with blood and surrounded by aggregation of inflammatory cells in small areas perhaps to the immune response (Fig. 8). These findings were maybe to effects of citric acid toxicity vessels caused hepatic degeneration in the liver parenchyma.

The histological result of the liver showed some hepatocytes were devoid of nuclei this may due to cell has undergone lyses leaving wide empty space and hemorrhage may be due to rupture of the vessel wall because of the dose of citric acid (Fig. 9). These histological changes of liver after treated with citric acid were agreement with Bakar and Aktac which noted the liver of rat when treated with food preservatives caused vacuolization and nucleus losses, hypertrophic hepatocyte, degeneration of hepatocytes, were seen in liver tissue these maybe to toxicity of citric acid lead to high damage in the liver.

**B. The Biochemical Results and Discussion**

**1. The results of the Level ALTand AST**

The result showed the level of ALT and AST in the serum of treated group mice that treated with citric acid were (441.0±14.0 U/L), (344.1±8.5 U/L) which have significantly increased compared with the control group (Tab. 2) . These results may be to a toxic effect of citric acid on liver tissue that caused acute degeneration of hepatocytes leads to an rise in the level of ALT and AST in current treated group with citric acid. These biochemical changes of ALT and AST enzyme after treated with citric acid were constant with Ortiz et al., and Aktaç et al [38].

**2. The Results of the Value of Serum Urea and Creatinine**

The results in (Tab. 2) showed the rate of serum urea and creatinine in mice treated group with citric acid were (34.00±0.97µm), (0.4271±0.014 mg/dl) which have significantly increased compared with control group. These results of high concentration of urea in the blood may be due to the gastrointestinal damage lead to hemorrhage which is associated with amplified protein intake (the blood in the gut is well a high protein meat) and thus increased urea production and consequently increased urea level. These physiological change of urea and creatinine after treated with citric acid were constant with [39] which showed an increase in the serum creatinine and urea level in the rats with increasing the dose of citric acid.

**Table 1.** The Diameter of Some Parameter of Histology Sections.

| Descriptive Statistics (N=40) Male | Control Group | Citric acid Group | Difference | 95% CI for Diff. | P-Value |
|---|---|---|---|---|---|
| | Mean± St. Dev | Mean± St. Dev | | | |
| Renal corpuscle | 22.92±0.55 | 24.45±0.48 | -1.524 | -2.968; -0.081 | 0.000* |
| Proximal convoluted tubules | 9.63±0.19 | 10.08±0.19 | -0.455 | -0.980; 0.069 | 0.000* |
| Distal convoluted tubules | 18.06±0.30 | 16.82±0.24 | 1.240 | 0.481; 2.000 | 0.000* |
| Descending limp | 9.64±0.15 | 10.171±0.13 | -0.531 | -0.927; -0.136 | 0.000* |
| Ascending limp | 12.18±0.17 | 12.59±0,17 | -0.414 | -0.867; 0.040 | 0.000* |
| Thickness of the liver capsule | 5.789±0.13 | 6.25±0.20 | -0.458 | -0.934; 0.018 | 0.000* |
| The diameter of hepatocyte nuclei | 8.595±0.10 | 8.793±0.12 | -0.198 | -0.507; 0.111 | 0.000* |

**Table 2.** Serum Creatinine, AST, ALT, and Urea of Mice.

| Descriptive Statistics (N=40) Male Enzyme | Control Group | Citric acid Group | Difference | 95% CI for Diff. | P-Value |
|---|---|---|---|---|---|
| | Mean± St. Dev | Mean± St. Dev | | | |
| Urea | 22.20±0.27 | 34.00±0.97 | -11.80 | -13.88; -9.72 | 0.000* |
| Creatinine | 0.36188±0.0016 | 0.4271±0.014 | -0.0652 | -0.0935; -0.0369 | 0.000* |
| AST | 273.75±0.40 | 344.1±8.5 | -70.35 | -87.56; -53.14 | 0.000* |
| ALT | 360.25±1.5 | 441.0±14 | -80.8 | -110.6; -50.9 | 0.000* |

Where:

- Two-sample T of control group and citric acid group
- Difference = mu (control group) – mu (citric acid group).
- *: refers to significance value.
- St.= Dev standard deviation
- AST (Aspartate Transaminase), ALT (Alanine Transaminase),

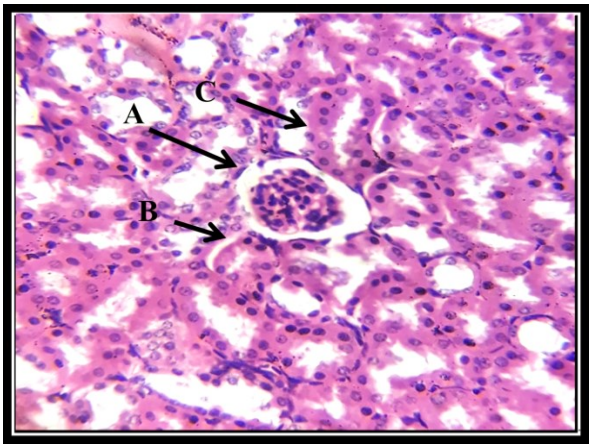


**Figure 1.** Transverse section of the kidney in control group which showed A-Renal corpuscle, B -Proximal convoluted tubule,C-Distalconvoluted tubule. H&E stain 40X.

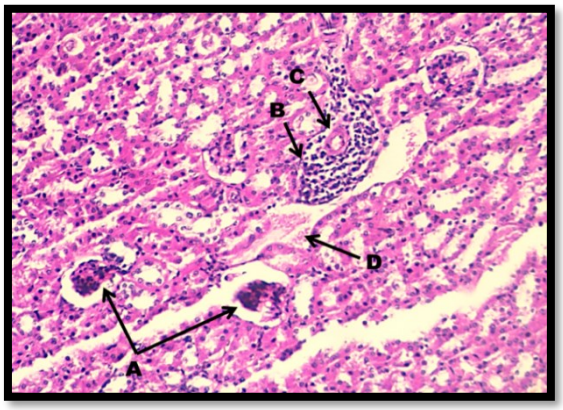


**Figure 2.** Transverse section of the kidney in treated group (citric acid) which showed A- Wide bowmans space, B-Aggregation of inflammatory cells, C-Vascular congestion, and D-Cystic dilation filled with blood. H&E stain 20X

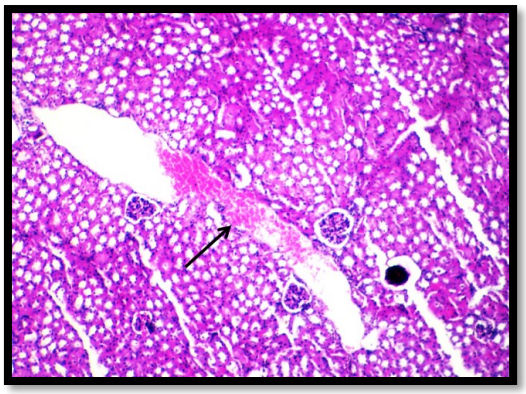

**Figure 3.** Transverse section of the kidney in treated group (citric acid) which showed long cystic dilation filled with blood (Black arrow). H&E stain 10X

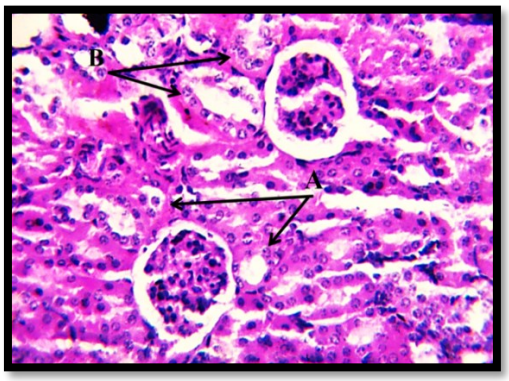


**Figure 4.** Transverse section of the kidney in treated group (citric acid) which showed A-Exfoliated epithelial layer of proximal convoluted tubules, B- Necrosis epithelial cells of distal convoluted tubules. H&E stain 40X.

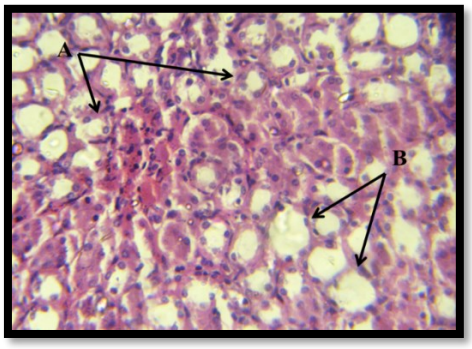


**Figure 5.** Transverse section of the kidney in treated group (citric acid) which showed Degeneration and Exfoliated epithelial layer of both A- Descending branched and B- Ascending branched. H&E stain 40X.

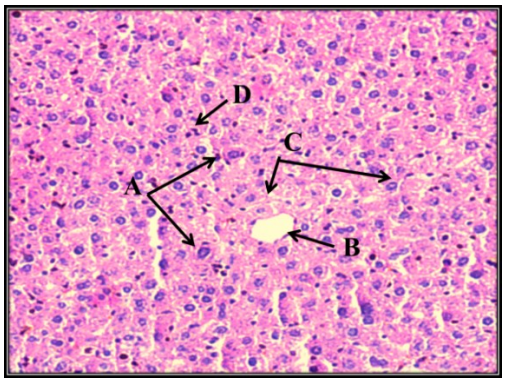


**Figure 6.** Transverse section of the liver in control group which showed A-Hepatocyte, B-Central vein, C-Sinusoids, D-Kupper cells H&E stain 20X.

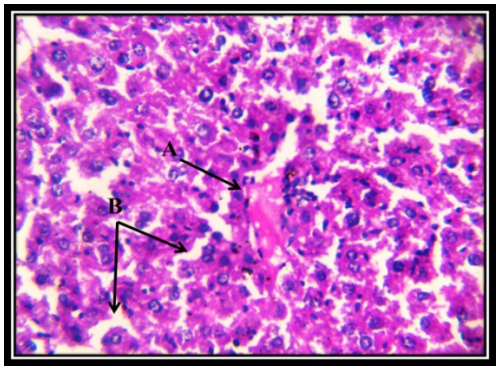


**Figure 7.** Transverse section of the liver in treated group (Citric acid ) which showed A- Damage in hepatic cord, B- Dilation in the sinuses with hemorrhage between sinusoid. H&E stain 40X.

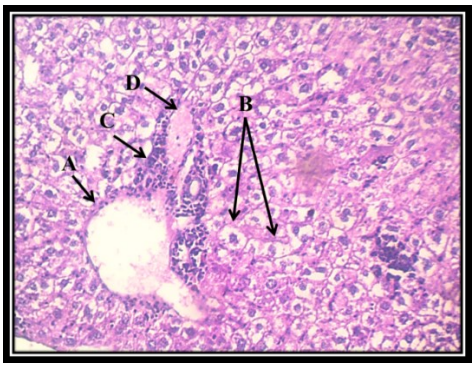


**Figure 8.** Transverse section of the liver in treated group (Citric acid) which showed A- Central vein, B- Enlargement of hepatocytes C-Aggregation of inflammatory cells D-Hemorrhage. H&E stain 40X.

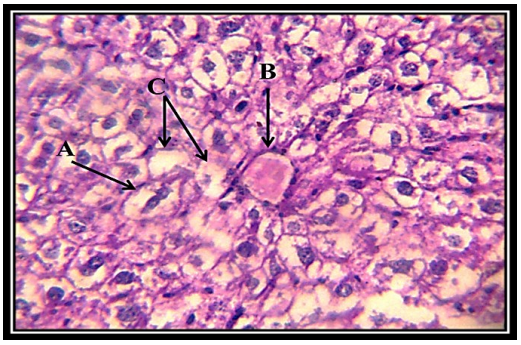


**Figure 9.** Transverse section of the liver in treated group (Citric acid) which showed A- Enlargement, and mitotic division in nuclei of hepatocytes, B- Hemorrhage in central vein, C- Hepatocytes lost nuclei. H&E stain 100X.

## IV. CONCLUSION

We conclude from the current study that citric acid at a concentration of 3% affects the kidneys, leading to bleeding between renal corpuscles, accumulation of inflammatory cells, expansion of blood-filled cysts, and peeling of the epithelial layer of the tubules, while its effect on the liver causes damage to the hepatic cords, a significant increase in the diameter of the nuclei of hepatic cells, accumulation of fatty materials in different areas of the liver, enlargement of hepatic cells, and expansion of sinusoids with bleeding.

The effect of citric acid on the biochemical results of both males and females showed a significant increase in the levels of ALT and AST, and a significant increase in the level of creatinine and urea was observed compared to the control groups, which indicated that food preservatives lead to an increase in the level of AST, ALT, creatinine, and urea in the treated group.

## REFERENCES

[1] H. A. Abdulmumeen, A. N. Risikat, and A. R. Sururah, "Food: Its Preservatives, Additives and Applications," International Journal of Chemical and Biochemical Sciences, vol. 1, pp. 36-47, 2012.

[2] F. A. Abushofa, A. E. Azab, and S. Alkadrawy, "Hepatic Pathophysiological Changes Induced by Nicotine and/or Sodium Nitrite Injection in Male Albino Rats," East African Scholars Journal of Medical Sciences, vol. 2, no. 4, pp. 184-196, 2019.

[3] T. Aktaç, A. Kaboğlu, E. Bakar, and H. Karakaş, "The Short-Term Effects of Single Toxic Dose of Citric Acid in Mice," Journal of Cell and Molecular Biology, vol. 2, no. 1, pp. 1-6, 2003.
[4] T. Aktac, A. Kaboglu, G. Kizilay, and E. Bakar, "The Short-Term Effects of Single Toxic Citric Acid Doses on Mouse Tissues: Histopathological Study," Journal of Cell and Molecular Biology, vol. 7, no. 1, pp. 35-42, 2008.
[5] A. M. Al-Harthy, A. Harib, A. J. Al-Shaaibi, S. S. Al-Toubi, and M. M. AbuKhader, "Food Additives Content in Selected Snack Foods and Beverages and Public Perception of E-Numbers in Muscat, Oman," Athens Journal of Health, vol. 4, no. 1, pp. 83-98, 2016.
[6] E. Al-Shammari, R. Bano, S. Khan, and I. Shankity, "The Effect of Preservatives and Flavour Additive on the Production of Oxygen-Free Radicals by Isolated Human Neutrophils," International Journal of Nutrition and Food Sciences, vol. 3, no. 3, pp. 210-215, 2014.
[7] S. Ameer, S. Aslam, and M. Saeed, "Preservation of Milk and Dairy Products by Using Biopreservatives," Middle East Journal of Applied Science & Technology (MEJAST), vol. 2, pp. 72-79, 2019.
[8] G. Assaf and S. El Khatib, "Thymol as a Natural Preservative in Cottage Cheese Preservation," EAS Journal of Nutrition and Food Science, vol. 3, no. 1, pp. 6-20, 2021.
[9] C. G. Awuchi, H. Twinomuhwezi, V. S. Igwe, and I. O. Amagwula, "Food Additives and Food Preservatives for Domestic and Industrial Food Applications," Journal of Animal Health, vol. 2, no. 1, pp. 1-16, 2020.
[10] E. Bakar and T. Aktaç, "Effects of Sodium Benzoate and Citric Acid on Serum, Liver and Kidney Tissue Total Sialic Acid Levels: An Ultrastructural Study," Journal of Applied Biological Sciences, vol. 8, no. 2, pp. 9-15, 2014.
[11] T. S. Banipal, N. Kaur, A. Kaur, M. Gupta, and P. K. Banipal, "Effect of Food Preservatives on the Hydration Properties and Taste Behavior of Amino Acids: A Volumetric and Viscometric Approach," Food Chemistry, vol. 181, pp. 339-346, 2015.
[12] A. Bearth, M. E. Cousin, and M. Siegrist, "The Consumer's Perception of Artificial Food Additives: Influences on Acceptance, Risk and Benefit Perceptions," Food Quality and Preference, vol. 38, pp. 14-23, 2014.
[13] S. Brul and P. Coote, "Preservative Agents in Foods: Mode of Action and Microbial Resistance Mechanisms," International Journal of Food Microbiology, vol. 50, no. 1-2, pp. 1-17, 1999.
[14] R. Chauer, "Sialic Acids: Fascinating Sugars in Higher Animals and Man," Zoology, vol. 107, no. 1, pp. 49-64, 2004.
[15] X. Chen, Q. Lv, Y. Liu, and W. Deng, "Effects of the Food Additive, Citric Acid, on Kidney Cells of Mice," Biotechnic & Histochemistry, vol. 90, no. 1, pp. 38-44, 2015.
[16] B. Dzigbordi, J. Adubofuor, and F. D. W. M. Faustina, "The Effects of Different Concentrations of Natamycin and the Point of Addition on Some Physicochemical and Microbial Properties of Vanilla-Flavoured Yoghurt Under Refrigerated Condition," International Food Research Journal, vol. 20, no. 6, pp. 3287-3292, 2013.
[17] A. M. El-Wakf, H. A. Hassan, F. G. El-Said, and A. El-Said, "The Association Between Prolonged Exposure to Water Nitrate Pollution and Increased Blood Methemoglobin Level in Both Young and Adult Male Rats," Journal of the Egyptian Society of Toxicology, vol. 49, pp. 91-96, 2009.
[18] B. Herr, "Additives in Dairy Foods: Types and Functions of Additives in Dairy Products," Dairy Foods Handbook, pp. 1-10, 2011.
[19] A. Heydaryinia, M. Veissi, and A. Sadadi, "A Comparative Study of the Effects of the Two Preservatives, Sodium Benzoate and Potassium Sorbate on Aspergillus niger and Penicillium notatum," Iranian Journal of Medical Microbiology, vol. 5, no. 3, pp. 32-39, 2011.
[20] M. A. Hussain, "Food Contamination: Major Challenges of the Future," Foods, vol. 5, no. 2, p. 21, 2016.
[21] M. J. Khoshnoud, A. Siavashpour, M. Bakhshizadeh, and M. Rashedinia, "Effects of Sodium Benzoate, a Commonly Used Food Preservative, on Learning, Memory, and Oxidative Stress in Brain of Mice," Journal of Biochemical and Molecular Toxicology, vol. 32, no. 2, e22022, 2018.

[22] C. L. Lawrence, C. H. Botting, R. Antrobus, and P. J. Coote, "Evidence of a New Role for the High-Osmolarity Glycerol Mitogen-Activated Protein Kinase Pathway in Yeast: Regulating Adaptation to Citric Acid Stress," Molecular and Cellular Biology, vol. 24, no. 8, pp. 3307-3323, 2004.
[23] B. G. Linke, T. A. Casagrande, and L. A. Cardoso, "Food Additives and Their Health Effects: A Review on Preservative Sodium Benzoate," African Journal of Biotechnology, vol. 17, no. 10, pp. 306-310, 2018.
[24] F. Mabood, J. Hussain, M. M. O. Al Nabhani, and S. A. Gilani, "Detection and Quantification of Formalin Adulteration in Cow Milk Using Near Infrared Spectroscopy Combined with Multivariate Analysis," Journal of Advanced Dairy Research, vol. 5, no. 2, pp. 1-6, 2017.
[25] D. M. Martyn, B. A. McNulty, A. P. Nugent, and M. J. Gibney, "Food Additives and Preschool Children," Proceedings of the Nutrition Society, vol. 72, no. 1, pp. 109-116, 2013.
[26] A. S. O. ME and M. S. M. Youssef, "Citric Acid Effects on Brain and Liver Oxidative Stress in Lipopolysaccharide-Treated Mice," Biomedicine & Pharmacotherapy, vol. 68, no. 2, pp. 221-229, 2014.
[27] S. K. Mirza, U. K. Asema, and S. S. Kasim, "To Study the Harmful Effects of Food Preservatives on Human Health," Journal of Medicinal Chemistry and Drug Discovery, vol. 2, pp. 610-616, 2017.
[28] J. N. Musyoka, G. O. Abong′, D. M. Mbogo, R. Fuchs, J. Low, S. Heck, and T. Muzhingi, "Effects of Acidification and Preservatives on Microbial Growth During Storage of Orange Fleshed Sweet Potato Puree," International Journal of Food Science, vol. 2018, no. 1, pp. 1-9, 2018.
[29] G. G. Ortiz, O. K. Bitzer-Quintero, C. B. Zárate, S. Rodríguez-Reynoso, F. Larios-Arceo, I. E. Velázquez-Brizuela, and S. A. Rosales-Corral, "Monosodium Glutamate-Induced Damage in Liver and Kidney: A Morphological and Biochemical Approach," Biomedicine & Pharmacotherapy, vol. 60, no. 2, pp. 86-91, 2006.
[30] M. Ritota and P. Manzi, "Natural Preservatives from Plant in Cheese Making," Animals, vol. 10, no. 4, p. 749, 2020.
[31] A. L. Robin and D. Sankhla, "European Legislative Framework Controlling the Use of Food Additives," Food Control Review, vol. 1, no. 1, pp. 1-12, 2013.
[32] O. Sacan, R. Yanardag, S. Bolkent, B. Bilgin-Sokmen, and S. Tunali, "Protective Effects of Selenium, Vitamin C and E Combination on Cadmium-Induced Toxicity in Various Tissues of Rats," Biological Trace Element Research, vol. 120, no. 1-3, pp. 234-241, 2007.
[33] K. Seetaramaiah, A. A. Smith, R. Murali, and R. Manavalan, "Preservatives in Food Products – Review," International Journal of Pharmacy and Biological Archives, vol. 2, no. 2, pp. 583-599, 2011.
[34] S. M. Shim, S. H. Seo, Y. Lee, G. I. Moon, M. S. Kim, and J. H. Park, "Consumers' Knowledge and Safety Perceptions of Food Additives: Evaluation on the Effectiveness of Transmitting Information on Preservatives," Food Control, vol. 22, no. 7, pp. 1054-1060, 2011.
[35] M. M. Silva and F. C. Lidon, "Food Preservatives: An Overview on Applications and Side Effects," Emirates Journal of Food and Agriculture, vol. 28, no. 6, pp. 366-373, 2016.
[36] M. M. Theron and J. F. Lues, "Organic Acids and Meat Preservation: A Review," Food Reviews International, vol. 23, no. 2, pp. 141-158, 2007.
[37] E. C. Yeung and P. K. Saxena, "Histological Techniques," in Protocol for Somatic Embryogenesis in Woody Plants, Dordrecht: Springer, pp. 517-537, 2005.
[38] S. Yılmaz, F. Ünal, D. Yüzbaşıoğlu, and H. Aksoy, "Clastogenic Effects of Food Additive Citric Acid in Human Peripheral Lymphocytes," Cytotechnology, vol. 56, pp. 137-144, 2008.
[39] F. Zamani Mazdeh, S. Sasanfar, A. Chalipour, E. Pirhadi, G. Yahyapour, A. Mohammadi, and M. Hajimahmoodi, "Simultaneous Determination of Preservatives in Dairy Products by HPLC and Chemometric Analysis," International Journal of Analytical Chemistry, vol. 2017, pp. 1-8, 2017.