ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 18, Issue, 01, pp.35858-35860, January, 2026
DOI: https://doi.org/10.24941/ijcr.50003.01.2026

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

EFFECTS OF ASPARTAME ON THE KIDNEY OF ADULT SWISS ALBINO MICE

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ARTICLE INFO

Article History:
Received 16th October, 2025
Received in revised form
12th November, 2025
Accepted 18th December, 2025
Published online 30th January, 2026

Keywords:
Asparteme, free radicals, cellulartoxicity, swiss albino mice, Histology.

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ABSTRACT

Background: Aspartame is a widely used non-nutritive sweetener, extensively consumed globally in low-calorie and sugar-free products. Despite its popularity, concerns remain regarding its long-term effects on human health, particularly renal function. **Objective:** This study was conducted to assess the histological and morphometric changes in the kidneys of adult Swiss albino mice following prolonged oral administration of aspartame. **Methods:** A total of 60 adult Swiss albino mice were divided into control (n=30) and experimental (n=30) groups. The experimental group received aspartame orally (100 µg/g body weight/day) for 8 weeks, while the control group received normal saline. Histological sections of kidneys were stained with Hematoxylin and Eosin, Masson's Trichrome, and Periodic Acid-Schiff stains. Microscopic and morphometric analyses were performed, and data were analyzed statistically. **Results:** The experimental group displayed significant renal histological alterations, including glomerular enlargement, increased Bowman's space, vacuolization of renal tubules, interstitial edema, and venous congestion. Morphometric data confirmed a statistically significant increase in renal corpuscle and glomerular diameter, and a reduction in cortical parenchymal volume proportion. **Conclusion:** Chronic aspartame intake induces notable histological and structural changes in the kidneys of mice, suggestive of nephrotoxicity. These findings raise concern regarding the long-term safety of aspartame consumption, especially in individuals with pre-existing renal conditions.

Citation: Dr. Vijay Gujar, Dr Karuna Kachhwa, Dr. Bhavna Khandve and Dr. Tarnekar, A.M. 2026. "Effects of aspartame on the kidney of adult swiss albino mice". ***International Journal of Current Research, 18, (01), 35858-35860.***

INTRODUCTION

Aspartame is a dipeptide methyl ester widely used as a low-calorie artificial sweetener, approximately 180 times sweeter than sucrose. It is commonly found in over 5,000 products including diet sodas, tabletop sweeteners, chewing gum, yogurt, and pharmaceutical syrups. Chemically, aspartame is composed of aspartic acid (50%), phenylalanine (40%), and methanol (10%)—each of which, upon metabolism, can exert physiological and potentially toxic effects. Aspartame's metabolic byproducts, especially methanol and its conversion to formaldehyde and formic acid, are well-documented for their toxic potential(Steginк, 1991; Oyama *et al*., 2002). Additionally, aspartic acid functions as an excitatory neurotransmitter, and excess phenylalanine may interfere with neurotransmitter synthesis(Parthasarathy *et al*., 2006). The kidney, being the primary organ for the excretion of many toxins and metabolic wastes, is particularly vulnerable to such exposures. Despite extensive safety evaluations by regulatory agencies, some studies suggest that long-term consumption of aspartame could pose health risks, particularly to renal and nervous systems. However, histological studies evaluating the structural changes in kidney tissue following prolonged aspartame consumption remain scarce.

Aims or Objectives: The present study aimed to explore the potential nephrotoxic effects of aspartame by conducting a comprehensive histological and morphometric analysis of kidneys in Swiss albino mice.

MATERIALS AND METHODOLOGY

Experimental Design: The present study was carried out in the departmental research lab of our institution. Prior approval of "Institutional Ethics Committee" and "Animal Ethics Committee" was duly obtained before starting the work. The basic study design was a histological case-control study based on experimentation on Swiss albino mice of two groups- cases and control.

Materials (Animal): A total of 60 adult Swiss albino mice nearly above 25 days, of both sexes were procured and acclimatized in laboratory conditions with standard 12-hour light/dark cycles, ambient temperature (20–25°C), and humidity (40–70%). Mice were housed in polypropylene cages with paddy husk bedding, fed a standard pellet diet, and provided clean drinking water ad libitum.

Grouping and Treatment

- **Group I (Control, n=30):** Received 1.25 ml normal saline daily via oral gavage.
- **Group II (Experimental, n=30):** Received 2.5 mg aspartame (100 µg/g b.w.) daily via oral gavage, dissolved in 1.25 ml normal saline. Aspartame was used in commercially available pellet form ("Sugarfree Gold"), and freshly prepared solution was administered at temperatures below 30°C.

Euthanasia and Sample Collection: After 8 weeks, mice were euthanized via intraperitoneal injection of thiopentone sodium (50 mg/kg body weight). Post-euthanasia, both kidneys were harvested, washed with saline, and fixed in 10% formal saline for 4–5 days.

Histological Processing and Staining: Kidney tissues were processed using standard paraffin embedding technique. Sections of 5–6 µm thickness were cut using a rotary microtome and stained with:

- Hematoxylin and Eosin (H&E) for general histology.
- Masson's Trichrome for collagen detection.
- Periodic Acid-Schiff (PAS) for glycogen and basement membrane visualization.

Microscopy and Morphometry

Slides were examined under light microscopy at magnifications of ×100, ×400, and ×1000. Morphometric measurements included:

- Diameter of renal corpuscles and glomeruli.
- Width of Bowman's space.
- Diameter of proximal and distal convoluted tubules.
- Volume proportion of cortical parenchyma vs. matrix.

A calibrated ocular micrometer and a square graticule (400 intersecting points) were used. Data were collected from at least 50 microscopic fields per sample.

Statistical Analysis: Data were analyzed using the Z-test. A p-value < 0.05 was considered statistically significant.

RESULTS

General Observations: Experimental mice showed early signs of lethargy, reduced appetite, and decreased responsiveness within 2–3 weeks of aspartame administration. Control mice remained active and healthy throughout the study.

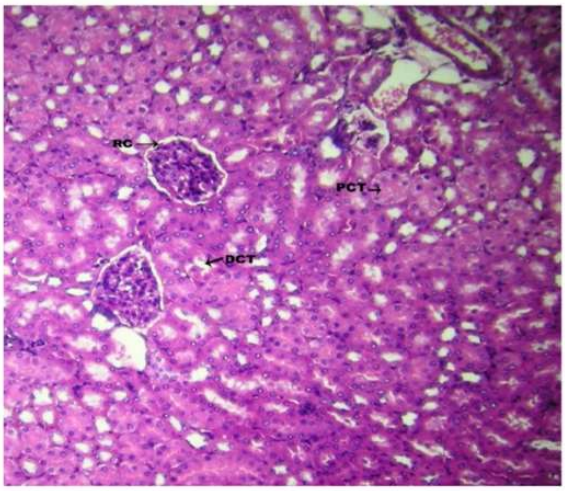
Weight Change: Experimental mice showed a mild reduction in net body weight gain compared to controls, but the difference was statistically insignificant ($z = 0.1867$, $p > 0.05$).

Gross Renal Appearance: There were no visible macroscopic differences in kidneys between the two groups. However, microscopic analysis revealed significant histological changes.

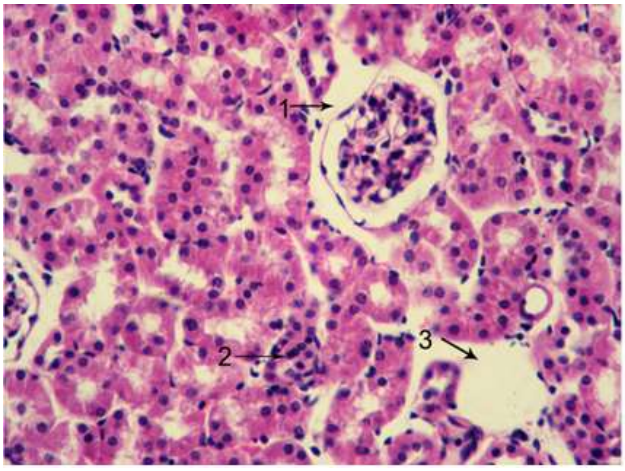
Histological Findings

Renal Cortex

- Pale staining of the renal cortex was noted, with enlarged luminal spaces of PCT and DCT.
- Epithelial lining showed reduced height and cytoplasmic vacuolation.
- Glomeruli were reduced in size in superficial cortical nephrons, with congested capillaries and vacuolated mesangial matrix.
- Some tubules were hyalinized with "ghost" outlines.
- Bowman's space was significantly widened; basement membranes were mostly intact as confirmed by PAS.
- Occasional fusion of Bowman's capsule with adjacent tubules was noted.
- Inflammatory cell infiltrate was mild; interstitial edema and vascular congestion were frequent.



Microphotograph 1. Cortex showing PCT, DCT, Cortical Nephron. (Control H& E 400)



Microphotograph 2: cortex showing interstitial edema,1-Interstitial matrix, 2- Tangentially cut glomerulus, 3-Dilated space around tubules. (Exp.H&E X 400)

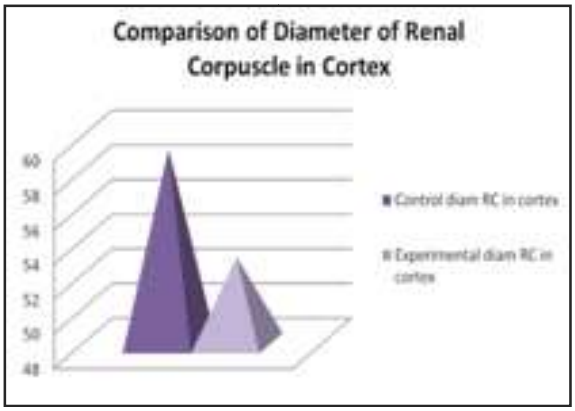


Fig. 1: Diagram of comparison of diameter of renal corpuscles in two groups

Juxtamedullary Region

- Glomeruli near the cortico-medullary junction maintained more regular structure.
- No evidence of hypercellularity or thickened basement membrane was observed.
- Tubules in this region appeared less affected compared to the superficial cortex.

Renal Medulla

- Collecting ducts and medullary tubules were dilated.
- Vasa recta showed marked vascular congestion.
- Interstitial areas were expanded; some tubules contained cellular casts.

DISCUSSION

The present study demonstrates significant histological and morphometric alterations in renal tissue following chronic oral administration of aspartame. Degenerative and fibrotic changes in both cortical and medullary regions support the hypothesis that aspartame may exert nephrotoxic effects. Bowman's space widening and glomerular dilation are indicative of impaired filtration and early glomerulonephritis, while the epithelial damage in tubules suggests disrupted reabsorption. Masson's trichrome staining revealed early interstitial fibrosis, confirming a progressive pathological process. These findings align with previous reports highlighting oxidative damage and glutathione depletion following aspartame exposure (Iman, 2011; Martins & Azoubel, 2007). The relative preservation of juxtamedullary glomeruli may reflect regional resistance or slower progression of injury. Overall, the renal pathology appears consistent with a toxic-metabolic etiology likely linked to aspartame metabolites (Oyama *et al*., 2002; Parthasarathy *et al*., 2006).

CONCLUSION

Prolonged exposure to aspartame induces significant structural and morphometric alterations in the kidneys of adult Swiss albino mice. These findings suggest nephrotoxicity involving glomerular and tubular components, likely mediated through oxidative and excitotoxic mechanisms. Further studies, particularly on human subjects and at varying dose ranges, are warranted to establish safe consumption thresholds.

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