Section: Anatomy

Original Research Article

HISTOLOGICAL EVALUATION OF ASPARTAME-INDUCED RENAL CHANGES IN ADULT SWISS ALBINO MICE

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ABSTRACT

Background: Aspartame is a widely used non-nutritive sweetener present in many low-calorie and sugar-free products. Despite its extensive use, concerns remain regarding its potential long-term effects on renal health. **Objective:** This study aimed to investigate the histological and morphometric changes in the kidneys of adult Swiss albino mice following prolonged oral administration of aspartame.

Materials and Methods: Sixty adult Swiss albino mice were randomly divided into control (n=30) and experimental (n=30) groups. The experimental group received aspartame orally at a dose of 100 µg/g body weight daily for 8 weeks, while controls received normal saline. Kidney tissues were processed and stained with Hematoxylin and Eosin, Masson's Trichrome, and Periodic Acid-Schiff. Histological and morphometric analyses were conducted, and data were statistically analyzed.

Results: The experimental group showed significant renal histological alterations, including reductions in the diameters of proximal and distal convoluted tubules and an increase in collecting duct diameters, along with venous congestion. Morphometric analysis revealed a significant increase in glomerular and renal corpuscle diameters and a reduction in cortical parenchymal volume.

Conclusion: Long-term aspartame intake induces notable structural and histological changes in mouse kidneys, suggesting potential nephrotoxicity. These findings raise concerns about the safety of chronic aspartame consumption, especially for individuals with pre-existing renal conditions.

Keywords: Aspartame; Renal Histology; Kidney Changes; Nephrotoxicity; Swiss Albino Mice; Histopathological Evaluation; Artificial Sweetener; Renal Tissue; Experimental Study; Adult Mice; Toxicological Study; Kidney Injury.

INTRODUCTION

Aspartame is a dipeptide methyl ester widely used as a low-calorie artificial sweetener, approximately 180 times sweeter than sucrose. It is present in over 5,000 products, including diet sodas, tabletop sweeteners, chewing gum, yogurt, and pharmaceutical syrups. Chemically, aspartame consists of aspartic acid (50%), phenylalanine (40%), and methanol (10%), each of which, upon metabolism, can exert physiological and potentially toxic effects. Specifically, methanol is metabolized to formaldehyde and formic acid, both of which are documented for their toxic potential (Stegink, 1991; Oyama et al., 2002). Aspartic acid functions as an excitatory neurotransmitter, and excess phenylalanine may interfere with neurotransmitter synthesis (Parthasarathy et al., 2006). Given that the kidney is the primary organ for excreting metabolic wastes and toxins, it 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, especially to renal and nervous systems.

However, histological investigations into structural kidney changes following prolonged aspartame intake are limited.

Aim: This study aims to comprehensively evaluate the histological and morphometric effects of chronic aspartame consumption on the kidneys of Swiss albino mice.

MATERIALS AND METHODS

Study Location and Ethical Approval: The study was conducted in the departmental research laboratory of our institution. Prior approval was obtained from the Institutional Ethics Committee and the Animal Ethics Committee before commencing the research.

Animal Model: A total of 60 adult Swiss albino mice, aged approximately 25 days and of both sexes, were acclimatized under standard laboratory conditions—12-hour light/dark cycle, temperature 20–25°C, and humidity 40–70%. Mice were housed in polypropylene cages with paddy husk bedding, fed a standard pellet diet, and had free access to clean drinking water.

Experimental Design and Treatment:

Group I (Control, n=30): Received 1.25 ml of normal saline daily via oral gavage.

Group II (Experimental, n=30): Received 2.5 mg aspartame (equivalent to 100 µg/g body weight) daily via oral gavage, dissolved in 1.25 ml normal saline. The aspartame used was commercially available ("Sugarfree Gold"), freshly prepared at temperatures below 30°C.

The treatment duration was 8 weeks.

Euthanasia and Sample Collection: At the end of the experimental period, mice were euthanized using intraperitoneal injection of thiopentone sodium (50 mg/kg body weight). Both kidneys were harvested, rinsed in saline, and fixed in 10% formal saline for 4–5 days.

Histological Processing and Staining: Kidney tissues were processed using standard paraffin embedding techniques. Sections of 5–6 µm thickness were cut with 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 basement membrane and glycogen visualization.

Microscopy and Morphometric Analysis: Slides were examined under light microscopy at magnifications of ×100, ×400, and ×1000. Morphometric parameters measured included:

Diameter of renal corpuscles and glomeruli.

Width of Bowman's space.

Diameter of proximal and distal convoluted tubules.

Volume proportion of cortical parenchyma versus interstitial matrix.

Measurements were performed using a calibrated ocular micrometer and a square graticule (400 intersecting points). Data were collected from at least 50 fields per sample.

Statistical Analysis: Data were analyzed using the Z-test, with a p-value < 0.05 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 ($z = 0.1867$, $p > 0.05$)

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.
- The mean value of the diameters of the PCT, DCT and collecting ducts of medulla were obtained.
- Glycogen content of tubules and stroma of kidney was largely unchanged as seen by PAS stained sections. The brush border of intact PCT and DCT demonstrated bright PAS positive reaction (figure 1 & 2)
- It is clearly evident from the table 8 that the diameters of the PCTs and DCTs were significantly reduced while there was a significant increase of diameters of collecting ducts in experimental set of kidneys. The relative increase in lumen of PCT and DCT and reduction of their diameters is indicative of renal tubular atrophy. Dilated collecting ducts with their wide lumina are indicative of urinary stasis in medulla.

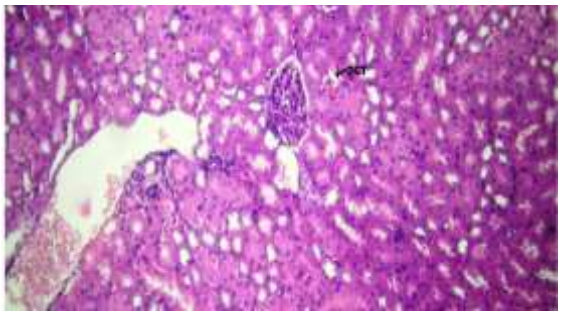

Figure 1: Real cortex showing PCT, DCT, & Cortical Nephron (Control.H&E X40)

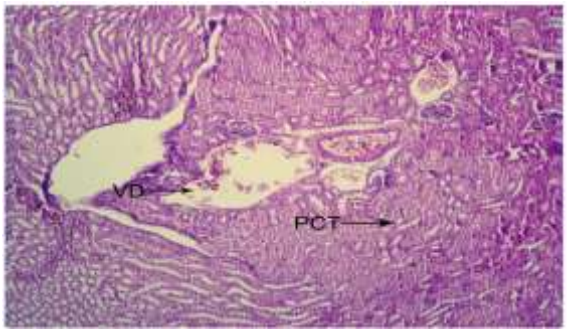

Figure 2: Real cortex showing early features of degeneration PCT & VD – Venous dilatation (Exp.H&E X40)

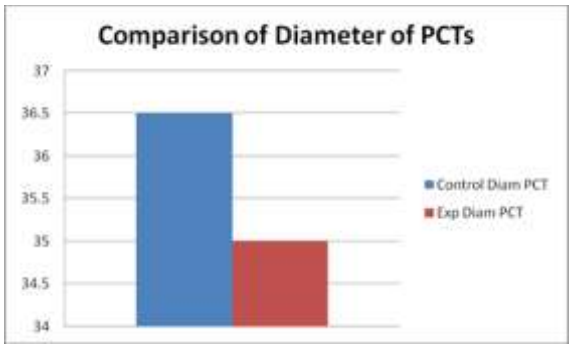

Figure 3: Diagram of comparison of diameters of PCTs (in µ) in two groups

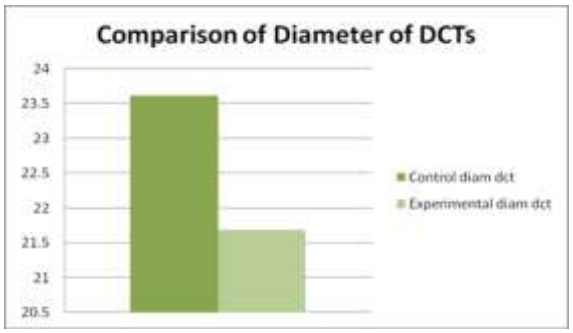

Figure 4: Diagram of comparison of diameters of DCTs (in µ) in two groups

DISCUSSION

This study reveals significant histological and morphometric alterations in renal tissue following chronic oral administration of aspartame, supporting its potential nephrotoxic effects. Degenerative and fibrotic changes in both cortical and medullary regions suggest adverse impacts on kidney structure. The renal damage is likely attributable to a negative anabolic effect and free radical-mediated toxicity, resulting in injury to the visceral epithelium (podocytes) and capillary endothelium of Bowman's capsule. Hydronephrotic changes may also occur due to partial obstruction of medullary tubules from venous congestion and interstitial nephritis.

While Martin et al. (2007) reported nuclear alterations in glomerular and tubular cells, along with a reduction in the proximal tubule brush border—findings that partially correspond with ours—Umi B. I. (2011) documented degenerative changes such as cloudy swelling, indicative of acute tubular damage. These features were rare in our study, suggesting a primarily compensated response to long-term aspartame exposure at the administered dose.

Overall, the observed renal pathology aligns with a toxic-metabolic etiology, likely linked to aspartame metabolites (Oyama et al., 2002; Parthasarathy et al., 2006).

CONCLUSION

Sustained 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. Diameters of PCT and DCT were reduced and that of collecting ducts were increased, all having statistical significance.

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