Uluslararası İleri Doğa Bilimleri ve Mühendislik Araştırmaları Dergisi
Sayı 9, S. 41-48, 4, 2025
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Araştırma Makalesi

IJANSER
https://as-proceeding.com/index.php/ijanser
ISSN:2980-0811

International Journal of Advanced Natural Sciences and Engineering Researches
Volume 9, pp. 41-48, 4, 2025
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Research Article

Histological study of reproductive organs in albino rats treated with Aspartame

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(Received: 5 April 2025, Accepted: 10 April 2025)

(3rd International Conference on Trends in Advanced Research ICSAR 2025, April 04-05, 2025)

ATIF/REFERENCE: Al-Jelawi, H. H. & Al-Essawi, D. A. H. (2025). Histological study of reproductive organs in albino rats treated with Aspartame. *International Journal of Advanced Natural Sciences and Engineering Researches*, 9(4), 41-48.

***Abstract* – Objective:** The study aimed to know the effect of the sweetener aspartame on the histological structure of the reproductive organs.

Methodology: the current study was conducted on 30 pregnant female rats, who were given oral doses of aspartame at a concentration of (8 mg/kg) starting from the zero day of the females' pregnancy until after birth. After that, the newborns (male and female) were separated from their mothers they were divided in to 3 equal groups, the G1: was considered a control group. The G2: included only male who were given oral doses of aspartame at a concentration of (8 mg/kg). the G3: included only female who were given oral doses of aspartame at a concentration of (8 mg/kg). each group ware dosed until reached puberty. after that the animals were sacrificed and the histological sections of the ovary and testis tissue were made .

Results: the histological sections results for testis tissue showed many changes where they included the appearance of destruction of sperm- producing cells, intratubular hemorrhage, degeneration of sperm-producing cells, seminiferous tubule atrophy, low sperms and scatter of sperm- producing cells., there were also changes in the histological composition of the ovary tissue represented by absence of most stages of ovarian follicle development, abundance atretic follicle, pulp tissue distraction, corpus luteum with granulocytes and occur bleeding in it and ovarian tissue destruction.

conclusion

Our study showed that the sweetener aspartame causes significant damage to the tissue structure of the reproductive organs in both the ovaries and testes after long-term consumption it.

Keywords – Aspartame, Sweetener, Ovary, Testis, Tissue.

I. INTRODUCTION

Aspartame was discovered in 1965 by James M. Schlatter, where Schlatter obtained this compound as part of research into antiulcer drugs. He invented the sweetness completely by fortuitous, after licking it off his finger, against work safety regulations, then aspartame began to be produced on a large -scale in 1981., white, odorless powder almost 200 times sweeter than sucrose, with a respective low calorific value. widely used in more than six thousand foods with under many brands names NutraSweet®, Equal®, Canderel®,

and Sugar Twin®. Aspartame is very much popular owing to its reduced costs, low caloric, attractive advertisements and assurance to contribute in weight management. The popularity of aspartame among consumers lies down within the problems associated with sucrose consumption, its presence in foods can be indicated either by name or by its code E951 [1].

Aspartame possesses the potential to serve as a constituent in a diverse array of comestibles and beverages, including but not limited to diet carbonated beverages, reduced-sugar fruit juices, and flavored aqueous solutions. Additionally, it has potential applications in the dairy industry, particularly in the production of light yoghurt and low-fat flavored milk. Furthermore, it can be utilized in the creation of nutrition bars, desserts such as sugar-free puddings and gelatins, as well as light ice cream and popsicles. Moreover, it can be incorporated into chewing gum, sauces, syrups, and condiments. Certain tabletop treats with reduced calorie content also contain aspartame as an ingredient. Additionally, it is crucial to acknowledge that aspartame is commonly incorporated into numerous prescription and over-the-counter medications, along with chewable pills, with the intention of enhancing their flavor and increasing customer appeal [2].

The acceptable daily intake (ADI) for aspartame is set at 40 mg/kg per days according to the European Food Safety Authority (EFSA), should be children and adults consumed it within the acceptable daily limit determined by the food and drug administration (FDA), because consumption in larger quantities than those recommended by the FDA, which may lead to serious health complications including headaches, migraines, cardiovascular disease, Alzheimer's disease, obesity and type 2 diabetes. [3].

II. MATERIALS AND METHOD

1. Animals for the experience

The study was conducted on 30 pregnant female albino rats- Sprague Dawley strain, Obtained from Faculty of veterinary medicine at Al- Kufa university then animals were transferred to the animal house located in the Department of Biology /College of Education for Girls/ University of Kufa, after that rats were placed in plastic cages covered with metal mesh covers, measuring 7× 15 × 48 cm. the cages were lined with sawdust, and the bedding was replaced twice a week, . in addition to regular cleaning and sterilization of the cages, the animals were left to acclimate in the animal house for 2 weeks before experiment. throughout all phases of the experiment, animals were kept under similar laboratory conditions, in clouding temperature, lighting, and humidity. they were provided with tap water and deep water designated for animals and feeding them with rough fodder obtained from laboratories specialized in manufacturing it during the experimental period. The experiment starting from the zero day of the females' pregnancy until the newborns reached the stage of maturity. the females continued to be dosed until after birth, i.e. during the lactation stage, until the newborns were weaned. After that, the newborns (male and female) were separated from their mothers and divided into three groups and dosed according to their body weight.

2. Preparing of the sweetener Aspartame

In this study, aspartame was used as a German-made colouring material agent, prepared by Al-Taif Office for Chemical Equipment/Baghdad - the name of the supplying company is Riedel Hean/Germany, it is know that the acceptable daily intake of aspartame in humans is 40 mg/kg body weight, so was calculated to be (8 mg/kg) for an average 200 gm weight rat, then animals was administered orally after dissolving them in 1 ml of distilled water for each concentration using a stomach tube (gavage device) as (LD 50) of oral aspartame is >10,000 mg/kg in rats [4].

3. Histological study

The histological study included the preparation of histological sections of the following organs: (Testis and Ovary), The samples were washed with water to remove the fixed formalin after that, the following steps were performed on them: Dehydration, Clearing, Infiltration, Embedding, Sectioning and Staining depending on the method of.[5].

III. RESULTS

The results of the microscopic examination showed histological changes of the Testis tissue in the groups, which were treated with concentration (8mg/kg) of Aspartame, where they included a group of changes as in figure (1-B), (1-C) and the figure (1-D). In addition, changes in ovary tissue were observed in the aspartame - treated groups concentration 8 mg as in figure (1-F), (1-G) and the figure (1-H).

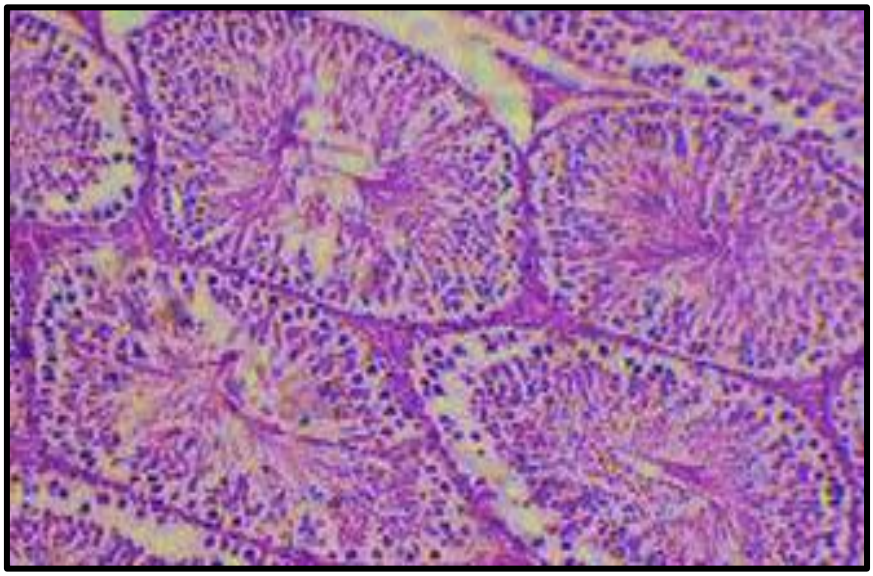

Figure. (1-A): A cross section of the testis of rat in the control group. (H&E 400X).

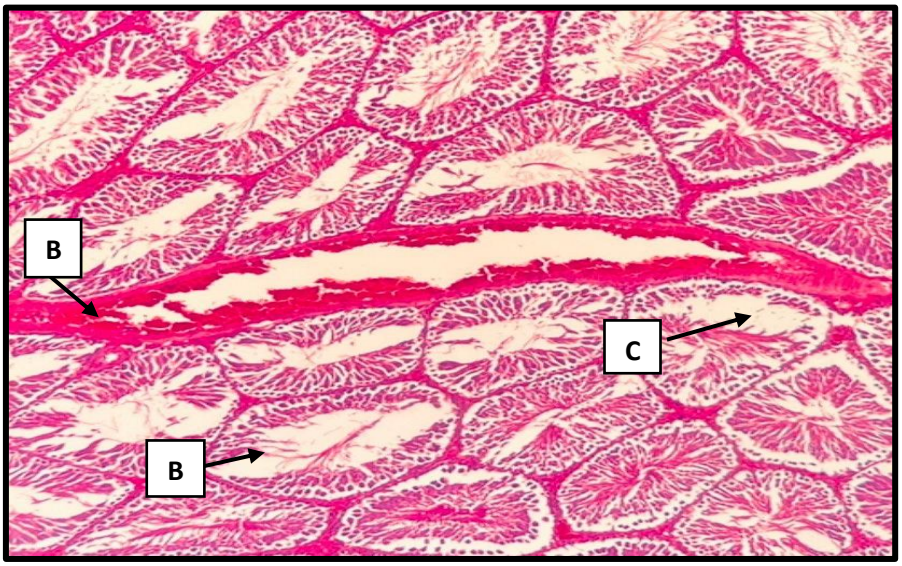

Figure. (1-B): A cross section of the testis of rat treated with aspartame concentration of 40 mg/kg, observed that **A:** Intratubular hemorrhage **B**: Less sperms **C:** Severe destruction of sperm- producing cells and atrophy of the seminiferous tubule space. (H&E 100X).

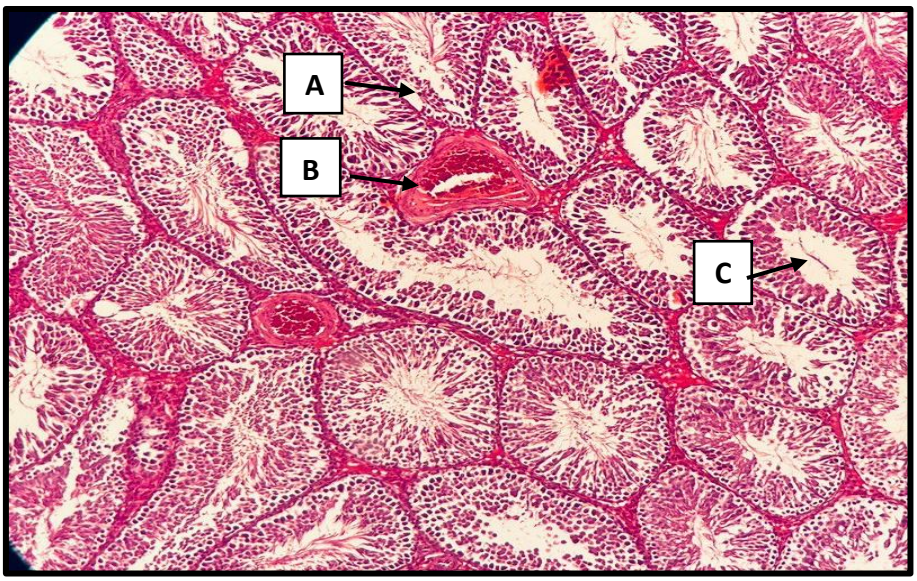

Figure. (1-C): A cross section of the testis of rat treated with aspartame concentration of 40 mg/kg, observed that **A:** degeneration of sperm-producing cells **B**: blood vessel enlargement and bleeding occur inside its **C:** Less sperms. (H&E 100X).

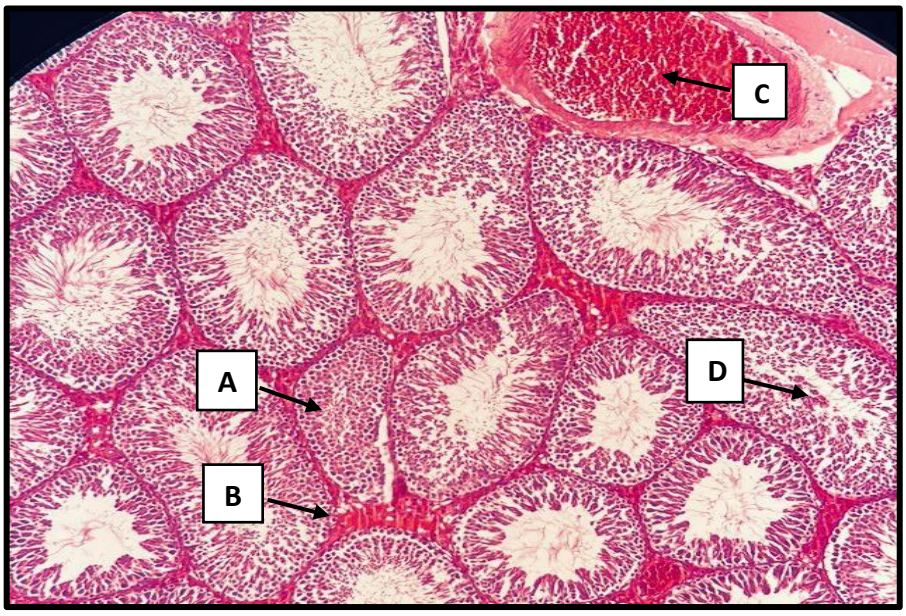

Figure. (1-D): A cross section of the testis of rat treated with aspartame concentration of 40 mg/kg, observed that **A:** Seminiferous tubule atrophy. **B**: hemorrhage **C:** Congestion **D**: low sperms and scatter of sperm- producing cells**.** (H&E 400X).

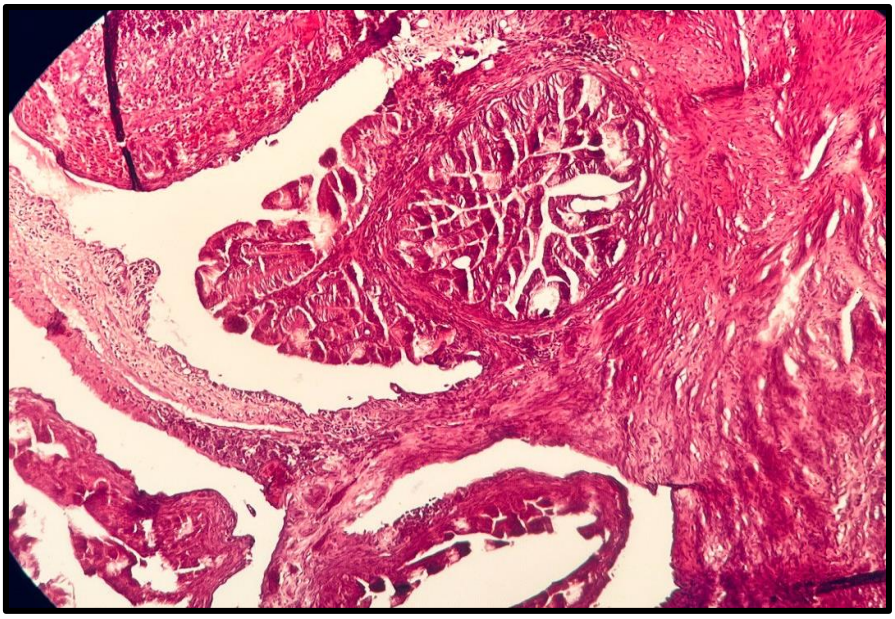

Figure. (1-E): A cross section of the ovary of rat in the control group (H&E 100X).

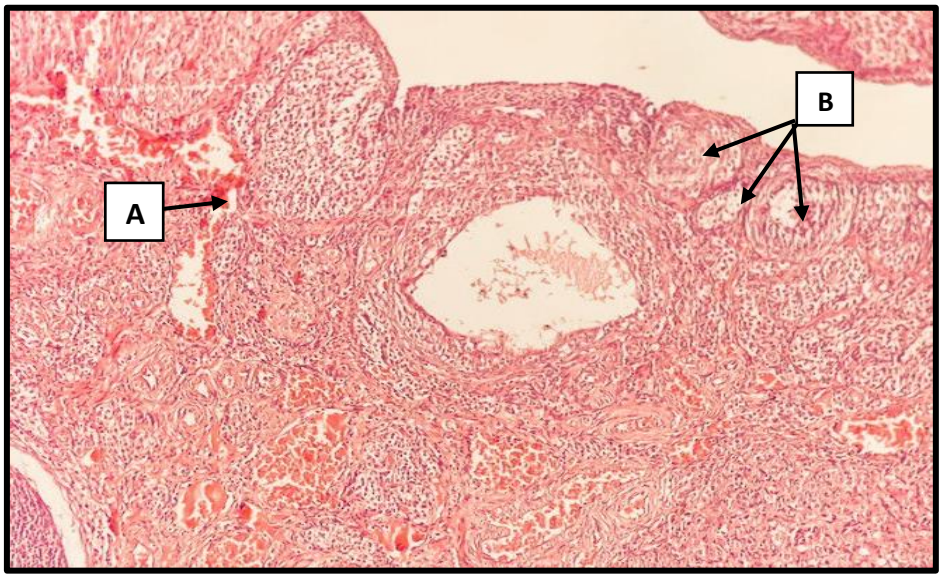

Figure. (1-F): A cross section of the ovary of rat treated with aspartame sweetener concentration of 40 mg/kg, observed the presence of **A:** Hemorrhage **B**: Abundance atretic follicle. (H&E 100X).

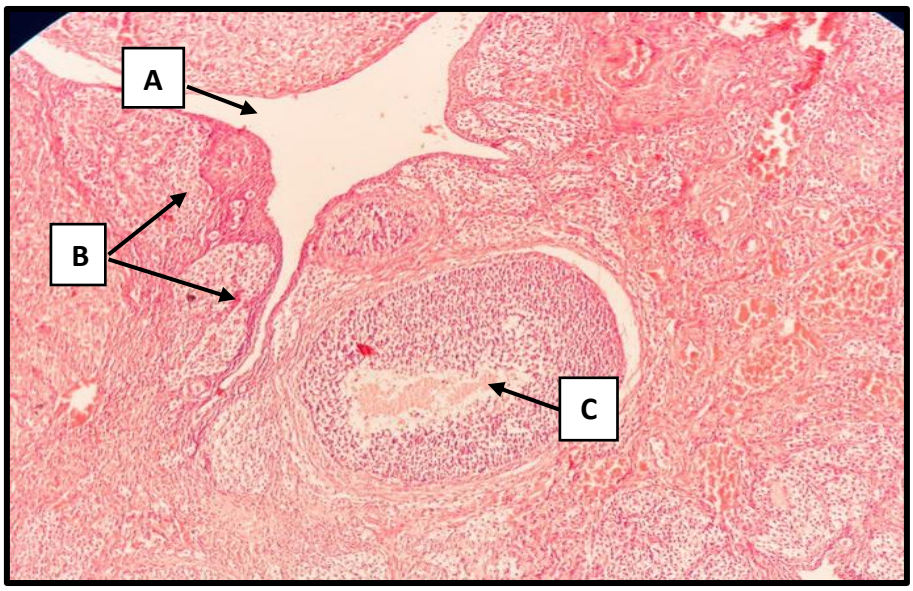

Figure. (1-G): A cross section of the ovary of rat treated with aspartame sweetener concentration of 40 mg/kg, observed the presence of **A:** Pulp tissue distraction **B**: Atretic follicle **C:** Corpus luteum with irregularly distributed granules. (H&E 100X).

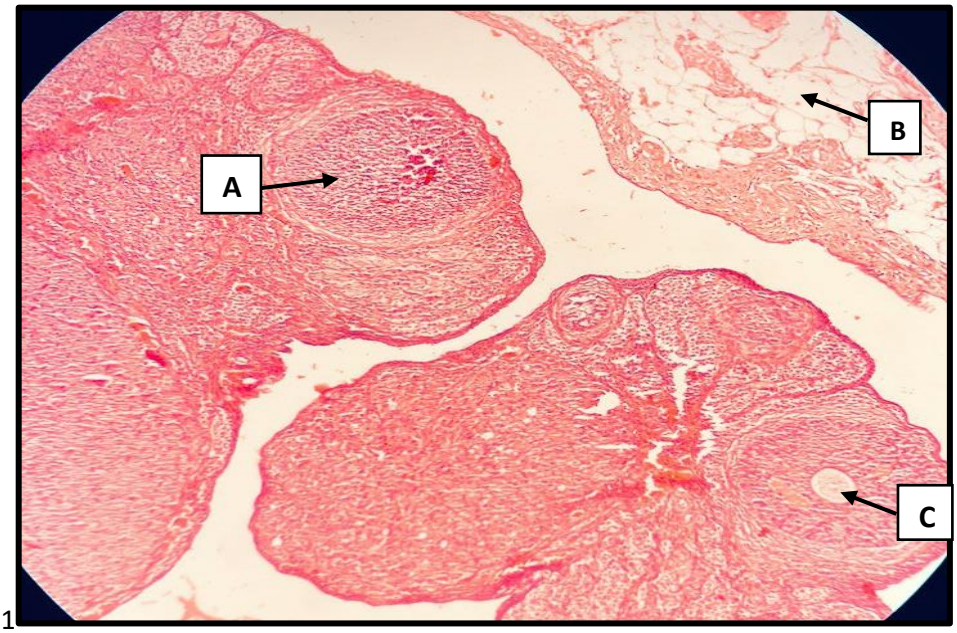

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Figure. (1-H): A cross section of the ovary of rat treated with aspartame sweetener concentration of 40 mg/kg, observed the presence of **A:** Corpus luteum with granulocytes and occur bleeding in it **B**: Ovarian tissue destruction **C:** Atretic follicle. (H&E 100X).

IV. DISCUSSION

The results of the histological examination showed the occurrence pathological tissue changes in the testis male rats' treated with aspartame at concentration (8mg/kg) , these changes including: destruction of sperm-producing cells, intratubular haemorrhage, less sperms and atrophy of seminiferous tubule space, degeneration of sperm- producing cells, seminiferous tubule atrophy, haemorrhage, low sperms, scatter of sperm- producing cells and blood vessel enlargement and bleeding occur inside its. The presence of congested blood vessels in the interstitial tissue indicated circulatory disturbances, which can impact testicular function. The results of the current study are consistent with the results of the study that revealed

the presence of male reproductive toxicity in a rat testis that consumed aspartame for a long period and at a dose exceeding the recommended safe dose, it showed reduce in sperm quality, disturbing antioxidant/oxidant levels reducing pituitary-testicular axis hormones concentration, and stimulating testicular cell apoptosis.[6]. Aspartame's toxicity may be due to the formation of more free radicals that resulting from methanol oxidation in the liver and thus the occurrence of oxidative stress that leads to damage to sperm DNA and inhibition of steroid synthesis in Leydig cells, or may be due to the ability aspartic acid and methanol of the two components resulting from aspartame metabolism in the intestine to cross the blood-testicular barrier which reduces sperm formation, reduced tubule size, spermatogenic arrest in the testis [7].

On the other hand, the results of this study are in clear contrast to the safety and usage recommendations put forth by the European Union, which recommended that aspartame and other sweeteners such as acesulfame-K, cyclamates, saccharin, sucralose, neo hesperidin DC (NHDC), neotame, the salt of aspartame-acesulfame, and advantage is safe for human consumption within the acceptable daily limits. (ADI).[8].

the current study revealed that treated with (8mg/kg) of aspartame sweetener resulted in significant alteration in the ovary causing haemorrhage, abundance atretic follicle, pulp tissue distraction, corpus luteum with irregularly distributed granules, corpus luteum with granulocytes and occur bleeding in it and ovarian tissue destruction, the results of the current study are consistent with those reported by Hosseini et al. [9] who reported that long-term exposure to aspartame causes severe histopathological changes in ovarian tissue, reduction in number of growing follicles, degenerative changes in follicular structure. Ali et al. [10]. also reported that oral administration of aspartame at a dose of (50 mg/kg) for 91 days to adult female albino rats caused decrease in serum estrogen as well as severe damage to ovarian tissue in form of decreased ovarian follicles, less mature graafian follicles, most cells showed vacuolations, haemorrhagic and necrotic foci with chronic inflammatory infiltrate and fibrosis. while other studies revealed a normal tissue structure in ovarian tissue and no pathological tissue changes were observed in the groups treated with aspartame. this contradicts our current study [11].

V. CONCLUSION

We conclude from our study that long-term use of aspartame, within acceptable limits, affects the formation of reproductive organs in both the ovaries and testes by causing numerous and clear histological changes, which affect the process of sperm formation, the growth of ovarian follicles, the formation of eggs, and consequently the fertilization process.

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