THE IRAQI JOURNAL OF
VETERINARY MEDICINE
eISSN:2410-7409
pISSN: 1609-5693

OPEN ACCESS

Evaluation of Some Male and Female Rats' Reproductive Hormones Following Administration of Aspartame With or Without Vitamin C or E

Omar H Azeez

Department of Pathology and Microbiology, College of Veterinary Medicine, University of Dohuk, Duhok, Duhok, Iraq

***Correspondence**:
omarvet@uod.ac

Received: 23 August 2021
Accepted: 4 October 2021
Published: 28 December 2021

DOI:
https://doi.org/10.30539/ijvm.v45i2.1256

Cite:
Azeez OH. Evaluation of some male and female rats' reproductive hormones following administration of aspartame with or without vitamin C or E. Iraqi J. Vet. Med. 2021; 45(2): 14-20.

A B S T R A C T

Aspartame (ASP) is a sugar substitute. Its use rose because it has been demonstrated to have deleterious effects after being metabolized. In the presence of antioxidant vitamins C or E, the effects of ASP on reproductive hormones of adult male and female Albino Wister rats were investigated. A total of eighty male and female rats were used in this study. The rats were divided into four groups: group 1, received no treatment; group 2, received ASP at 40 mg/kg BW; group 3, received ASP at 40 mg/kg BW with vitamin C at 150 mg/kg BW; and group 4, received ASP at 40 mg/kg BW and vitamin E at 100 mg/kg BW. All treatments were given orally by gavage needle once daily for consecutive 90 days. The levels of estradiol (E2), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone hormone (TH) were measured after 90 days in blood plasma. In comparison with the control group, ASP treatment resulted in lower levels of E2, FSH, and LH in male and female rats. When the antioxidants vitamin C or E was given, the effects of ASP were reversed, and the levels of E2, LH, and FSH were increased. The testosterone hormone was likewise significantly increased by ASP, but testosterone hormone concentrations were decreased by vitamin C or E treatments. Long-term ASP consumption caused interfering with testicular and ovarian hormonal activity, while vitamins C and E on the other hand, overcome longstanding consumption ASP's effects.

Keywords: aspartame, estradiol, LH, FSH, testosterone

INTRODUCTION

Intense, non-nutritive, or low-calorie sweeteners are all terms used to describe artificial or alternative sweeteners (1). It is a flavor enhancer that works in the same way as sugar does. As a result, they are known as sugar alternatives (2). Therefore, food items containing sweeteners other than sugar are grown in popularity. Artificial sweeteners are sparked the creation of sugar-free goods, notably in diabetes, energy restriction, special diets, and obesity (3). Saccharine, acesulfame-K, aspartame (ASP), cyclamate, neotame, and sucralose are the most prevalent artificial sweeteners (4).

ASP is one of the most often used artificial sweeteners. It was developed in 1969 and has 200 times of the sweetening power of table sugar. It is utilized in over 6000 (food and beverage) items due to its excellent sensory characteristics. Tabletop sweeteners, soft drinks, chewable multi vitamins, morning cereals, dessert mixes, yogurt, frozen desserts, and medicines all include it (5). In addition, ASP is frequently utilized in weight loss and hygiene goods (6). As ASP degrades into its constituent amino acids,

phenylalanine and aspartic acid, its shelf life shortens, making it an unattractive sweetener in baking (7). Because of its propensity for toxicity, ASP is the most controversial artificial sweetener, causing a variety of health issues (8). It is harmful to a wide range of tissues and organs, including the liver (9). Similarly, long-term ASP treatment is shown to enhance lipid peroxidation and nitric oxide levels, resulting in the generation of free radicals that disrupt homeostasis. In mice and rats (10), ASP inhibits the production of reproductive hormones by lowering the levels of LH, FSH, and testosterone (11). Vitamins C and E, on the other hand, are antioxidants that may decrease the consequences of oxidative stress-related testicular dysfunction in animal tissues. Vitamins C and E are antioxidants, and tocopherols are involved in reducing the effects of free radicals on proteins and cell membranes (12).

The objective of this paper is to determine the effect of chronic ASP administration on sex hormone (males and females) using Albino Wistar rats as an *in vivo* model, as well as to look into the potential role of vitamin C (vit C) and vitamin E (vit E) in reducing the negative effects of ASP.

MATERIALS AND METHODS

Animals

Eighty adult, male and female Wistar rats (3-4 months old) weighing 200-325 g were utilized. Animals were maintained in the animal house at the College of Veterinary Medicine, University of Duhok. The rats were maintained in cages in a room with a well-ventilated temperature (22±2 °C) and were subjected to 12-hour light/12-hour dark cycles. The rats were provided with a normal pellet diet for rats. Food and drink were freely available. All animals were handled and treated according to laboratory animal care and use protocols (13). The Animal Ethics Committee at the College of Veterinary Medicine, University of Duhok, Iraq originally gave its approval to the study.

Chemicals

The aspartame was purchased from Alfa Aesar Thermo Fisher Scientific, Germany, while vit C was bought from Scharlau, Spain and vit E from Extrasynthese, France.

Experimental Design

Adult Albino Wistar rats were utilized to study the effects of long-term ASP intake on the reproductive system hormones of both male and female rats in the presence of antioxidants vitamins C and E. The rats (males and females) were divided into four groups, each of which included 20 rats (10 males and 10 females). The rats in group 1 were given simply distilled water as a control. The rats in group 2 were given 40 mg/kg BW of ASP which was dissolved in distilled water; the dosages were determined based on the acceptable daily intake (ADI) (40 mg/kg) (14). In group 3, the rats were given 40 mg/kg BW ASP plus 150 mg/kg BW of vit C (15), and in group 4, the rats were given ASP at 40 mg/kg BW plus 100 mg/kg BW of vit E (16). Over the course of 90 days, all of the treatments were administered orally by gavage once daily.

Collection of Samples

Blood samples (3 mL) were taken from the orbital venous plexus of the treated and control groups (17). The samples were taken at two separated times: at the beginning of the study and after 90 days of therapy. Blood samples were taken in a tube containing EDTA anticoagulant, and the blood samples were transported in a cooled box to the biochemistry lab at the College of Veterinary Medicine, University of Duhok, Iraq, for hormone measurements.

Hormonal Assays

The enzyme linked immunosorbent assay (ELISA) method was used to determine the plasma levels of luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone hormone (TH), and estradiol in using a standard ELISA kit (MyBioSource, USA) specific for rats and following the manufacturer's instructions.

Statistical Analysis

SPSS (IBM SPSS; version 22.0, IBM Corp., Armonk, NY, USA) software was used to analyze the collected data. One-way analysis of variance (ANOVA) was used to examine all of the data. The Duncan multiple range test was used to detect specific differences between the groups (18). The acceptable significance threshold was $P \leq 0.05$. The mean and standard error of the mean (SEM) of rats (n = 10) per group were used to calculate the results. Changes in percentage were also calculated.

RESULTS

Effect of ASP Consumption on Male Rat Reproductive Hormones for 90 Days in the Presence of Vit C or E

Figure1A indicates that ASP had no effect on E2, but ASP combined with vit C resulted in considerable increases of E2 (24% and 31%, respectively) when compared to the control group or the ASP-treated group.

The level of FSH was reduced by 25% after ASP treatment, however in the presence of either vit C or E, the level of FSH recovered to normal levels when compared to the control group, and there was a substantial rise in FSH level when compared to the ASP group by 38% and 24%, respectively (Figure1B).

Figure 2A shows the impact of ASP or in combination with vit C or E on plasma LH levels in male rats. ASP alone

substantially lowered the amount of LH by 25%, but ASP with vit C or E had no action when compared to the control group, whereas ASP with vit C or E significantly increased the level of LH by (48%) and (20%), respectively.

Plasma testosterone levels of rats in ASP group alone increased by 34%, whereas rats in ASP+vit C or vit E groups lowered by 28% and 46%, respectively, when compared to the control group or the ASP-treated group (Figure 2B).

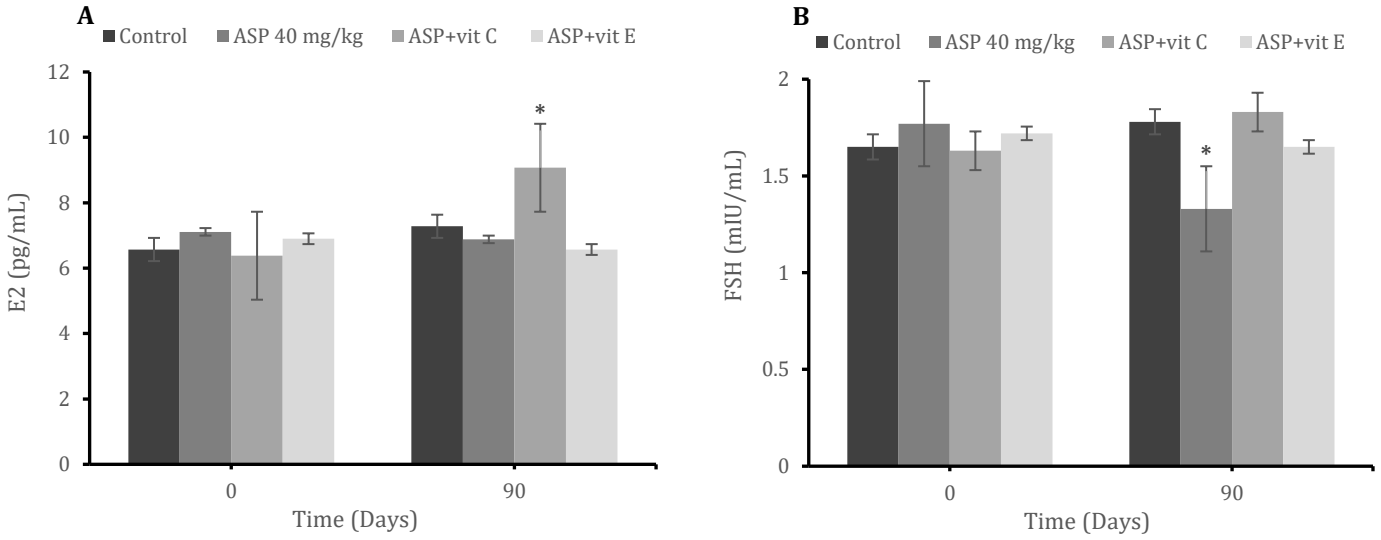

Figure 1. **A)** Plasma estradiol (E2), and **B)** follicle-stimulating hormone (FSH) levels of Albino Wister male rats administred aspartame (ASP) at 40 mg/kg BW for 90 days and treated with vitamin C (ASP+vit C) at 150 mg/kg BW and vitamin E (ASP+vit E) at 100 mg/kg BW. The values are expressed as mean±SEM, n=10. Significant level (*) was considered at $P \leq 0.05$ compareing to control

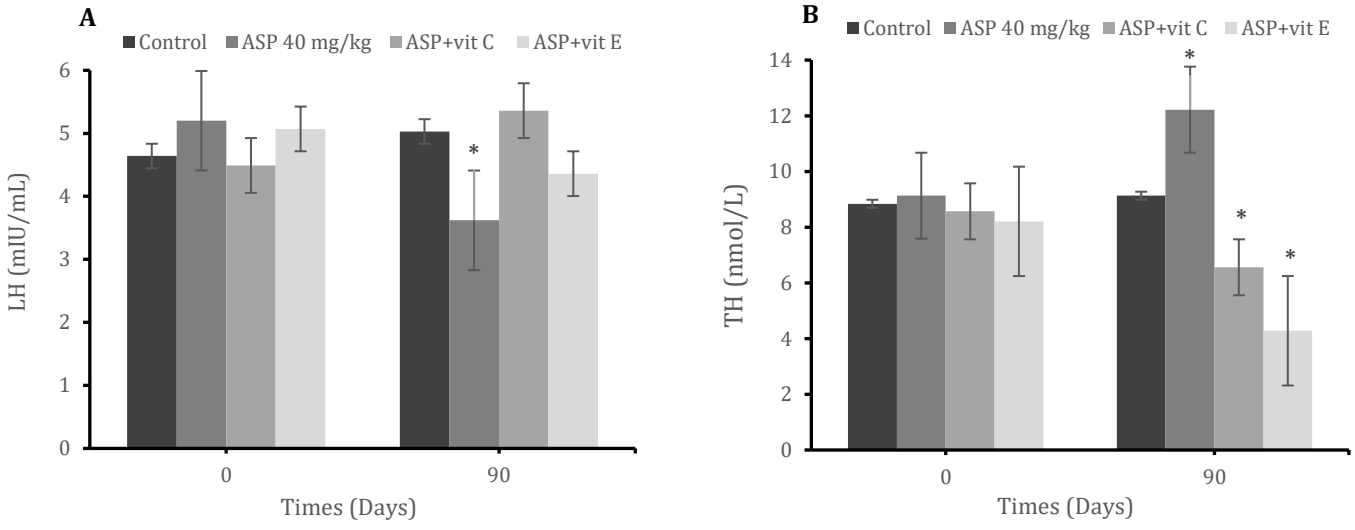

Figure 2. **A)** Plasma luteinizing hormone (LH), and **B)** testosterone hormone (TH) levels of Albino Wister male rats administred aspartame (ASP) at 40 mg/kg BW for 90 days and treated with vitamin C (ASP+vit C) at 150 mg/kg BW and vitamin E (ASP+vit E) at 100 mg/kg BW. The values are expressed as mean±SEM, n=10. Significant level (*) was considered at $P \leq 0.05$ compareing to control

Effect of ASP Consumption on Female Rat Reproductive Hormones for 90 Days in the Presence of Vit C or E

When ASP was given alone, the level of E2 in female rats increased by 16 %; however, when vit C was added, the level of E2 decreased by 9% to the ASP group. When compared to the control and ASP groups, ASP and vit E reduced significantly E2 levels by 17% and 29%, respectively (Figure 3A).

Figure 3B depicts the effect of ASP on FSH levels in the blood. In rats treated with ASP alone, the level of FSH was decreased by 29%. In addition, as compared to the control and ASP groups, ASP+vit C resulted in substantial reductions in FSH levels of 21% and 12%, respectively.

In comparison to the control group, ASP alone reduced blood LH levels by 36%, whereas ASP+vit C reduced LH levels by 20%. When compared to the ASP group, the amount of LH increased by 12%. When comparing the ASP

group to the ASP+vit C group, the female rats treated with ASP+vit C also had a substantial rise in blood LH levels of 76% (Figure 4A).

In comparison to the control group and the ASP alone treated rats, the effect of ASP alone on the plasma level of testosterone in female rats was significant, reducing testosterone by 28%; however, testosterone was found at normal levels in ASP treated rats in the presence of vit C, whereas testosterone was found at normal levels in ASP treated rats in the absence of vit C (Figure 4B).

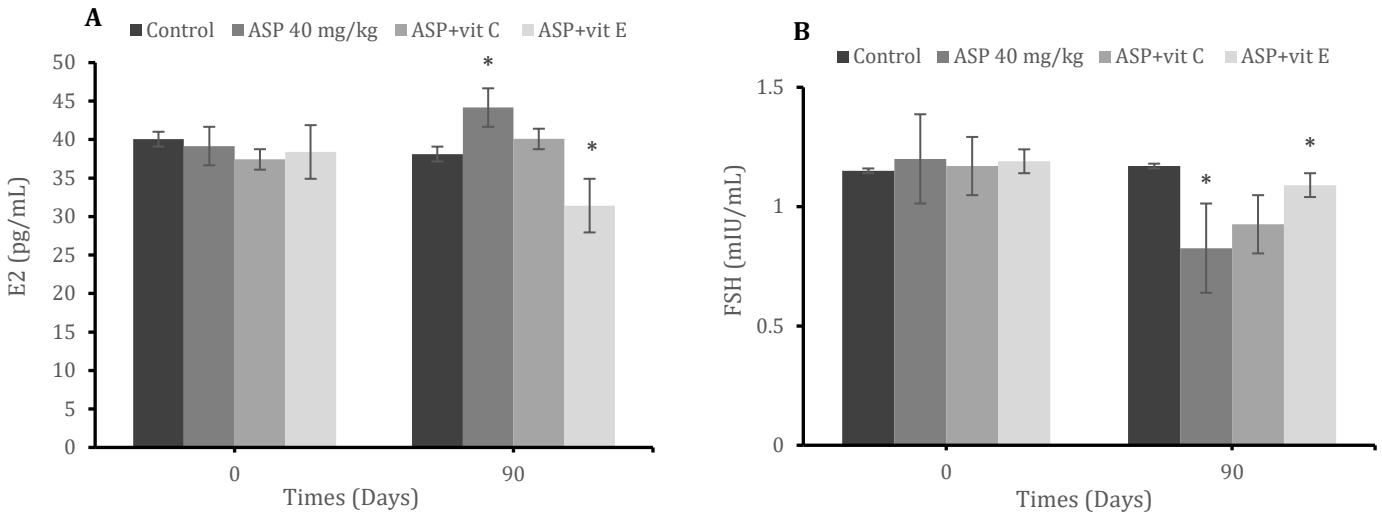

Figure 3. **A)** Plasma estradiol (E2), and **B)** follicle-stimulating hormone (FSH) levels of Albino Wister female rats administred aspartame (ASP) at 40 mg/kg BW for 90 days and treated with vitamin C (ASP+vit C) at 150 mg/kg BW and vitamin E (ASP+vit E) at 100 mg/kg BW. The values are expressed as mean±SEM, n=10. Significant level (*) was considered at $P \leq 0.05$ compareing to control

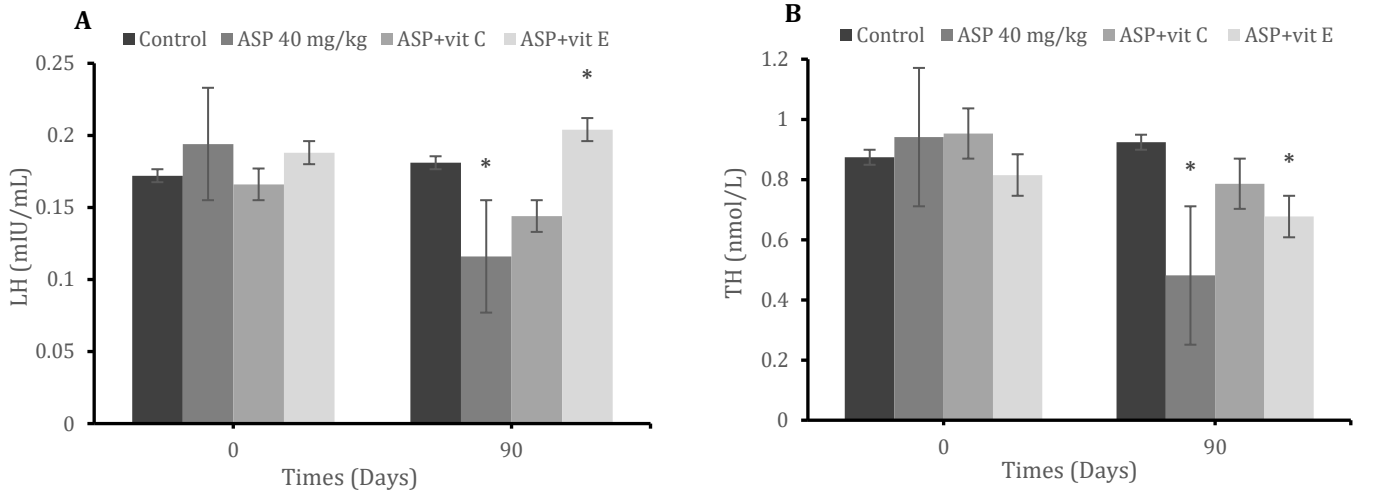

Figure 4. **A)** Plasma luteinizing hormone (LH), and **B)** testosterone hormone (TH) levels of Albino Wister female rats administred aspartame (ASP) at 40 mg/kg BW for 90 days and treated with vitamin C (ASP+vit C) at 150 mg/kg BW and vitamin E (ASP+vit E) at 100 mg/kg BW. The values are expressed as mean±SEM, n=10. Significant level (*) was considered at $P \leq 0.05$ compareing to control

DISCUSSION

The results of this study showed that administering ASP to male rats resulted in a substantial drop in FSH, LH, and estrogen levels, which was consistent with prior research (11, 19). Significant reductions in LH, testosterone, and FSH concentrations were found in the treatment groups as compared to the control group in their research. According to Ashok et al. (20), the metabolites produced in ASP breakdown in the body are aspartic acid, phenylalanine, and methanol, then methanol breakdown to formaldehyde and formate, the effects of ASP on the reproductive systems of rats can be linked to methanol metabolism, which results in the toxicity of hazardous metabolites that enhance oxidative stress and impair sperm quality (20). Their findings showed that methanol metabolism in rats resulted in lower sperm count and viability, as well as higher levels of glutathione-s-transferase (GST) and glutathione

peroxidase, as well as the harmful role of ASP metabolism in inducing oxidative stress in epididymal sperms and influencing sex hormones (20). Anbara et al. (21) conducted an experimental study to evaluate the effects of ASP consumption on the reproductive system in male mice, found significant differences in the levels of oxidative stress and testosterone stress biomarkers and sperm parameters in the control and experimental groups (21) and concluded that long-term ASP consumption is harmful to the reproductive system as a result of oxidative stress induction. Similarly, Razi et al. (22) found that formaldehyde poisoning had a substantial impact on the levels of reproductive hormones, sperm viability, and spermatogenesis in rats, potentially leading to male infertility. Methanol oxidation impairs the function and structure of proteins that control and maintain the lower temperatures of the testes in the male reproductive system (23). Furthermore, antioxidants have an effect on the fluidity of sperm plasma membranes and the integrity of DNA in the sperm nucleus (24). Reactive oxygen species (ROS) cause DNA damage by speeding up cell death and lowering sperm cell counts, both of which are indications of male infertility (25).ROS attack polyunsaturated fatty acids on sperm membranes, causing remodeling of the biophysical properties and composition of the sperm membranes by altering their electron stability, membrane potential, and energy production capacity, which affects the production of reproductive hormones by the testes and ovaries (26). El-Haliem (27) found that ASP treatment causes enlargement of most cells in the pars distalis and causes histological alterations in the pituitary-thyroid axis in adult male albino rats, as well as reduced pituitary hormone production. Additionally, Puica et al. (28) found that prolonged treatment of ASP to white Wistar rats at the pre-pubertal stage caused neurodegenerative consequences, particularly in the hypothalamus, as well as significant structural and functional changes in the hypothalamic-pituitary axis. This changed hormone concentrations, resulting in reduced production of gonadotropin-releasing hormone (GnRH), LH, and FSH, as well as suppression of testosterone synthesis and secretion, resulting in a reduction in reproductive capability. Also, due of the impacts on the structure and function of the heat shock proteins (HSPs), ASP intake and subsequent methanol poisoning are hypothesized to produce endocrine changes in the reproductive system (HSPs). These HSPs have a function in regulating spermatogenesis and cytoprotective actions, as well as increasing cell resilience to environmental stresses (29). Antioxidants, on the other hand, lower the chance of developing or progressing a variety of illnesses induced by oxidative stress, such as male and female infertility owing to testicular dysfunction and sperm production, as well as diminished reproductive hormone production (30). Vitamins C and E have antioxidant properties, which means they decrease the consequences of oxidative stress-related testicular abnormalities in animal tissues (31). Vitamin C protects cells by decreasing oxidative stress-induced cellular damage caused by (ROS), whereas vit E protects proteins from alkylation caused by electrophilic lipid peroxidation by neutralizing hydroperoxyl radicals (32). Vitamin E scavenges hydroperoxyl radicals in the lipid milieu, reducing free radical effects on proteins and cell membranes, as well as DNA damage, and so reducing oxidative stress in the body (33, 34). Additionally, by awarding electrons to active free radicals to extinguish their effectiveness, lowering oxidative stress either through antioxidant scavenging activity or by restoring antioxidant enzyme efficacy to normal levels, reducing oxidative stress (35). Reduced free radical effects on proteins and cell membranes, as well as the ovaries and testes, resulted in less oxidative stress in the body and improved reproductive hormone production (36). The findings of this study, which showed that vitamins C and E can reverse the effects of ASP on estradiol, LH, and FSH levels, are similar with those of previous investigations. Ali et al. (37), for instance, found that vit C protects the testes from the toxicity of ASP. Anbara et al. (38), who studied the effects of vit C on hemolytic anemia caused by phenylhydrazine (PHZ), discovered that vit C had antioxidant properties. Vitamin C substantially decreased mRNA damage, increased the quality of sperm produced, testicular antioxidant and endocrine condition, and encouraged embryo pre-implantation development (38).

When compared to the control group, ASP treatment resulted in lower levels of estrogen, FSH, and LH, as well as higher levels of testosterone in rats. Vitamins C and E, on the other hand, were discovered to mitigate ASP's effects. The compounds that caused toxicity and elevated oxidative stress in the testicular and ovarian tissues, as well as reducing their function, were blamed for the impacts of ASP on reproductive hormones. To minimize adverse effects on the reproductive system, non-nutritive sweeteners should be consumed or used in moderation.

ACKNOWLEDGEMENTS

The author is grateful to the help given by the College of Veterinary Medicine, University of Duhok specially the staff of the research center.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

1. Ni Y, Xiao W, Kokot S. A differential kinetic spectrophotometric method for determination of three sulphanilamide artificial sweeteners with the aid of chemometrics. Food Chem. 2009; 113(4): 1339–1345.

2. Chattopadhyay S, Raychaudhuri U, Chakraboty R. Artificial sweeteners – A review. J Food Sci Technol. 2014; 51(4): 611-621.
3. Pinheiro MVS, Oliveira MN, Penna ALB, Tamime AY. The effect of different sweeteners in low-calorie yogurts: a review. Int J Dairy Techn. 2005; 58: 193–199.
4. Dietrich AM, Pang Z, Zheng H, Ma X. Mini Review: Will artificial sweeteners discharged to the aqueous environment unintentionally "sweeten" the taste of tap water? Chem Eng J Adv. 2021: 100100.
5. Zafar T, Naik QAB, Shrivastava VK. Aspartame: Effects and awareness. MOJ Toxicol. 2017; 3(2):1-5.
6. Alleva R, Borghi B, Santarelli L, Strafella E, Carbonari D, Bracci M, et al. In vitro effect of aspartame in angiogenesis induction. Toxicol. In-Vitro. 2011; 25(1): 286–293.
7. Hooda R, Sharma M, Sharma M. Aspartame determination in soft drinks. IJREST. 2015;2(4): 41-44.
8. Harpaz D, Yeo LP, Cecchini F, Koon THP, Kushmaro A, Tok A, et al. Measuring artificial sweeteners toxicity using a bioluminescent bacterial panel. Molecules. 2018; 23(10): 1-20.
9. Finamora I, PérezaS, Bressanb CA, Brennerb CE, Rius-Péreza S, Brittesc PC, et al. Chronic aspartame intake causes changes in the trans-sulphuration pathway, glutathione depletion and liver damage in mice. Redox Biol. 2017; 11:701–707.
10. Anbara H, Sheibani MT, Razi M, Kian M. Insight into the mechanism of aspartame-induced toxicity in male reproductive system following long-term consumption in mice model. Environ Toxicol. 2020; 36(2): 223-237.
11. Al-Salamy A, Al-Awady H. Effect of different doses of aspartame on the male reproduction hormones concentration in rats. Plant Arch. 2019;19(s2): 1830-1832.
12. Sadaghiani S, Fallahi S, Heshmati H,Teshnizi SH, ChaijanHAb, Amir Ebrahimi FF, et al. Effect of antioxidant supplements on sperm parameters in infertile male smokers: A single-blinded clinical trial. AIMS Public Health. 2020;7(1): 92-99.
13. Gnadt J. Ethical and Legal Perspectives. In: Suckow MA, Weisbroth SH, Franklin CL, editors. The Laboratory Rat. A volume in American College of Laboratory Animal Medicine. 2nd edition. USA: Elsevier Academic Press; 2006. p.53-70.
14. Renwick GA. "The intake of intense sweeteners–an update review". Food Addit Contam. 2006; 23 (4): 327–38.
15. Abdelaziz I, Ashour AERA. Effect of saccharin on albino rats'blood indices and the therapeutic action of vitamins C and E. Hum Exp Toxicol. 2011; 30(2): 129-137.
16. Shati AA. Ameliorative effect of vitamin E on potassium dichromate-induced hepatotoxicity in rats. J King Saud Univ Sci. 2014; 26(3): 181–189.
17. Fox JG, Cohen BJ, Loew FM. Laboratory Animal Medicine. U.K: Academic press London; 1984. 19-120.48 p.
18. Bruning JL, Kintz BL. Computational Handbook of Statistics.2nd edition. Illionois USA: Scott Foresman and Co. Glenveiw;1977. 75-80,102-138 p.
19. Hozayen WG, Soliman HE, Desouky EM. Potential protective effects of rosemary extract, against aspartame toxicity in male rats. J Inter Acad Res Multidisc. 2014; 2(6): 111-125.
20. Ashok I, Poornima P, Wankhar D, Ravindran R, Sheeladevi R. Oxidative stress evoked damages on rat sperm and attenuated antioxidant status on consumption of aspartame. Int J Impot Res. 2017; 29(4): 164-170.
21. Anbara H, Sheibani M, Razi M. Long-term effect of aspartame on male reproductive system: Evidence for testicular histomorphometrics, Hsp70-2 protein expression and biochemical status. Int J Fertil Steril. 2020; 14(2): 91-101.
22. Razi M, Malekinejad H, Sayrafi R, Hosseinchi MR, Feyzi,Moshtagion SM, Janbaz H. Adverse effects of long-time exposure to formaldehyde vapor on testicular tissue and sperm parameters in rats. Vet Res Forum. 2013; 4(4): 213-219.
23. Kregel KC. Heat shock proteins: modifying factors in physiological stress responses and acquired thermotolerance. J Appl Physiol. 2002; 92(5): 2177-2186.
24. Agarwal A, Saleh R, Bedaiwy M. Role of ROS in the pathophysiology of human reproduction. Fertil Steril. 2003; 79(4): 829-843.
25. Wagner H, Cheng J, Ko E. Role or ROS in male infertility: An updated review of literature. Arab J Urol. 2018; 16(1): 35-43.
26. Nowicka-Bauer K, Nixon B. Molecular changes induced by oxidative stress that impair human sperm motility. Antioxidants (Basel). 2020; 9(2): 134.
27. El-Haliem NG. The effect of aspartame on the pituitary thyroid axis of adult male albino rat and the possible protective effect of Pimpinella-anisum oil: histological and immune-histochemical study. Egy J Histo. 2013; 36(1): 195-205.
28. Puica C, Craciun C, Rusu M, Cristescu M, Borsa M, Roman I. Ultrastructural aspects of the hypothalamus-pituitary complex reactivity following chronic administration of aspartame in juvenile rats. Stu Univ Sci Ser. 2009; 19(1): 19-24.
29. Shamsi-Gamchi N, Razi M, Behfar M. Testicular torsion and reperfusion: Evidences for biochemical and molecular alterations. Cell stress chaperones. 2018; 23(3): 429-439.
30. Sharifi-Rad M, Kumar N, Zucca P, Dini L, Panzarini E, Rajkovic J, et al. Lifestyle, oxidative stress and antioxidants: Back and forth in the pathophysiology of chronic diseases. Front Physiol. 2020; 11: 694.
31. Saddein E, Haghpanah T, Nematollahi-Mahani S, Seyedi F, Ezzatabadipour M. Preventative effects of vitamin E on testicular damage and sperm parameters in the first-generation mice pups due to pre- and post-natal Mancozeb exposure. J Toxicol. 2019; 2019: 1-12.
32. Traber M, Stevens J. Vitamins C and E: Beneficial effects from a mechanistic perspective. Free Radic Biol Med. 2012; 51(5): 1000-1013.
33. Niki E. Evidence for beneficial effects of vitamin E. 2015. Korean journal of internal medicine 2015; 30(5): 571-579.
34. Assumaidaee AAM, Ali NM, Fadhil AA. Effect of vitamin E as α-tocopherol acetate on mercuric chloride-induced chronic oxidoreductive stress and nephrotoxicity in rats. Iraqi J. Vet. Med. 2019; 43 (2): 102-112.
35. Al-Jammas S, Al-Saraj A. The histological changes induced by Cytarabine on rabbits livers (with and without vitamin E administration). Iraqi J Vet Sci. 2020; 34(1):9-13.
36. Asadi N, Bahmani M, Kheradmand A, Rafieian-Kopaei M. The impact of oxidative stress on testicular function and the role of antioxidants in improving it: A review. J Clin Diagn Res. 2017; 11(5): IE01-IE05.
37. Ali W, Mohamed S, Abdallah E, El-Deen E. Protective effect of vitamin C against aspartame toxicity to the testes: A review article. Sohag Med J. 2019; 23(2): 52-55.
38. Anbara H, Shahrooz R, Razi M, Malekinejad H, Najafi G. The effects of vitamin C on mice hemolytic anemia induced by phenylhydrazine: An animal model study using histological changes in testis, pre-implantation embryo development, and biochemical changes. Iran J Basic Med Sci. 2018; 21(7): 668-677.

تقييم بعض الهرمونات التناسلية لذكور وإناث الجرذان بعد اعطاء الأسبارتام (السكرين) مع أو بدون فيتامين ج أو هـ

عمر حسن عزيز

فرع الأمراض والأحياء المجهرية، كلية الطب البيطري، جامعة دهوك، دهوك، العراق

الخلاصة

الأسبارتام (Aspartame) هو من السكريات الصناعية. هناك مخاوف بشأن استمرار استخدامه حيث ثبت أن له آثارًا سلبية بعد عملية التمثيل الغذائي داخل الجسم. قيمت هذه الدراسة آثار الأسبارتام على هرمونات الجهاز التناسلي لكل من ذكور وإناث الجرذان في وجود مضادات الأكسدة: كُل من فيتامين ج أوهـ. تم استخدام ثمانون من ذكور وإناث جرذان Wister والتي تراوح أوزنها بين 200-325غم، وزعت الجرذان المستخدمة عشوائياً إلى أربع مجموعات. كانت المجموعة الاولى مجموعة سيطرة ولم تتلق أي علاج، فيما تلقت المجموعة الثانية الأسبارتام بتركيز 40 ملغم / كغم من وزن جسم ، وتلقت المجموعة الثالثة الأسبارتام بنفس التركيز مع فيتامين (ج) بتركيز 150 ملغم / كغم من وزن جسم ، وتلقت المجموعة الرابعة الأسبارتام بنفس التركيز مع فيتامين (هـ) عند 100 ملغم / كغم من وزن جسم. تم إعطاء جميع العلاجات عن طريق الفم بواسطة الانبوب المعوي لمدة 90 يوماً، وتم تقييم مستويات هرمون الاستراديول (E2) والهرمون اللوتيني (LH) والتستوستيرون والهرمونات المنشطة للجريب (FSH) في بلازما الدم. تسبب استهلاك الأسبارتام على المدى الطويل في حدوث تسمم وزيادة الإجهاد التأكسدي في أنسجة الخصية والمبيض ، بالإضافة إلى تقليل وظيفتها، ومن ناحية أخرى كان لفيتامينات (ج) و (هـ) الأثر في التخفيف من آثار الأسبارتام.

الكلمات المفتاحية: الأسبارتام، هرمون الاستراديول، الهرمون اللوتيني، الشحمون الخصوي