The effect of Aloe Vera gel on some physiological parameters in white female rats exposed to Bisphenol A

Mohammed Jameel Mohammed1, Ahmed Salahaldeen Mohealdeen1, Ali Hussein Jameel1 and Hind Abdel Aziz1

1Department of Food Sciences, College of Agriculture, Tikrit University, Iraq.

Email: m_jamel68@yahoo.com

Abstract

The aim of this study was to evaluate the effect of oral administration of Aloe vera gel 20 % in laboratory rats that exposed to Bisphenol A at a concentration of (10, 20) mg/kg on its body weight and biological parameters after a period of 28 days. Results showed a significant decrease (P <0.05) in the body weight of groups of rats given Bisphenol A orally. The values of uric acid, creatinine, and urea were significantly increased, there was also a significant increase in the activity of all values of the enzymes ALT, AST, and ALP. Giving an additional quantity of aloe vera gel by drinking water with the presence of Bisphenol A had a significant effect in reducing the negative impact of Bisphenol A on weight, biochemical, and enzymatic parameters.

Key words: Aloe Vera, Bisphenol A, Physiological parameters.

1. Introduction

Medicinal plants possess many therapeutic and medicinal properties such as antioxidant action [1]. Aloe vera is a semi-tropical plant of the Liliaceae family which has a wide range of applications in traditional medicine [2]. It has been widely used in many fields, including cosmetic and health care products, and at present, it is used for therapeutic purposes, the gel has been used as an antibacterial and antifungal [3] and antiviruses [4]. While its effects as an antioxidant increased its use more and more broadly, in addition to the use of aloe vera in stimulating the immune system and treating cancerous tumors and intestinal disorders [5]. This plant is characterized by its thick, fleshy leaves with needle tips and spiny edges, in addition to containing a gel rich in many active substances that act as antimicrobial agents for pathogenic bacteria [6]. Moreover, this plant has anti-disease effects and contains many nutrients that can drive the metabolism process, such as Entraquitone group, and many minerals, vitamins, amino acids, and enzymes [7].

According to [8] chemical composition of the aloe vera plant consists of polyphenol saponins (Intraketone), and minerals such as (calcium, potassium, chromium, manganese, zinc, sodium, magnesium, copper, and choline), and vitamins such as B1, B2, B6 E, A, folic acid, beta-carotene, monosaccharides and amino acids. Aloe vera is a factor influencing oxidase, amylase and lipase enzymes, and is used as an antibiotic [9]. Aloe vera has over 75 nutrients and 200 active compounds including sugar, anthraquinones, saponins, vitamins, enzymes, minerals, lignin, salicylic acid and amino acids, and other different potentially active compounds including water-soluble and fat-soluble vitamins, minerals, enzymes, simple/complex polysaccharides, phenolic compounds, and organic acid [10]. Throughout the globe, many plants have been utilized for their medicinal properties. Aloe vera species has been used in folk medicine for over 2000 years and has remained an important component in the traditional medicine of many countries, the ingredients responsible for the beneficial effects of this plant are present in leaves. It is commonly called "Guar patha" or Ghee-Kuar [11]. Bisphenol A is a polycarbonate or epoxy resin chemical that is commonly used in the manufacture of many consumer products such as food and beverage containers and water bottles [12]. The upper limit for the permissible daily intake of BPA as recommended by the US Environmental Protection Agency and European food safety authorities is in the range of 0.05 mg / kg of body weight per day [13]. Several studies have confirmed that exposure to bisphenol is associated with various disorders of the proliferative system [14]. Bisphenol acts as a reproductive toxicant and causes a real risk to humanity as it weakens fertility in humans in general [15]. [16] reported a decrease in the weight of rats with all treatments of the used concentrations of BPA. [17] reported an increase in the level of liver enzymes for both ALT and AST and...
an increase in the concentration of uric acid. Food is the most important method of exposure of humans to bisphenol by eating canned food and drinking water as the filtration of bisphenol from the plastic lining of cans of drinks and food. The filtration of bisphenol from plastic is increased when it is cleaned with a strong detergent or when it contains acidic liquids or high temperatures and is also used in the manufacture of epoxy gum used in coating water tanks [18]. Bisphenol A is one of the most important substances that interfere with hormone function [19]. The study aimed to evaluate the effect of oral administration of Aloe vera gel in laboratory rats that exposed to Bisphenol-A at on its body weight and some biological parameters.

2. Materials and methods

2.1. Preparation of the aqueous extract of Aloe Vera

The aqueous extract of aloe vera gel was prepared by taking (100 grams) of the gel after sterilization, removing the outer cover of aloe vera’s leaf and collecting gel with a spoon, weighting by a sensitive balance, and mixing with a liter of boiling distilled water using a mixer device for a period of (5-7) minutes and leaving the extract for (6-8) hours at room temperature before use [20, 21].

2.2. Bisphenol A

Bisphenol A was obtained from an Indian company named; Alpha Chemica. It was dissolved in Olive oil and orally administered to the laboratory animals at a concentration of (10, 20) mg/kg body weight.

2.3. Preparation of laboratory animals

The laboratory animals were obtained from the College of the Veterinary Medicine / University of Tikrit. It was Albino Sprague-Dawley weanling adult female rats at the age of 8-9 weeks with a weight average of 140-165 gm. The total of adult animals were 25 animals which were randomly divided into 5 groups, each group contained 5 animals, which was separately treated with one of the following treatments:

- Control (distilled water only).
- Bisphenol A at a concentration of 10 mg/kg.
- Bisphenol A at a concentration of 20 mg/kg.
- Aloe Vera 20% + Bisphenol A at a concentration of 10 mg / kg.
- Aloe Vera 20% + Bisphenol A at a concentration of 20 mg / kg.

The experimental animals were kept in the animal house under temperature of 20-25 °C and lighting duration of not less than 12 hours a day. Its food was prepared according to [22] and regularly provided during the period of the experiment of 28 days. The initial weight was taken after one day of solitary feeding of the animals, and the weight gain was obtained by calculating the difference between the initial weight and the final weight as per following formula:

\[ \text{Final Weight} - \text{Initial Weight} = \text{Weight gain (g)} \]

2.4. Blood tests

These tests were conducted immediately at the end of the experiment period, targeted animals were starved for 20 hours, anesthetized with chloroform, and sacrificed from the neck area according to [23]. For drawing the blood needed for the necessary tests, approximately 6-8 ml of blood were drawn in gel tubes, centrifuged using a centrifuge at 3000 rpm for 15 minutes to obtain the serum, which was kept at -20 ° C until the analyzes were carried out [24].

2.5. Statistical analysis

Complete Random Design (CRD) was applied in this experiment with five replicates and its data were subjected to the analysis of variance test (ANOVA) through the Linear Model General within the ready-made statistical program [25]. The averages of evaluated traits were compared according to [26] multiple tests at (0.05) level.
3. Results and discussion

3.1. The effect of Alo Vera on body weight

Table 1 shows the effect of adding Bisphenol A to rat’s drinking water at a concentration of (10, 20) mg/kg for 28 days on its body weight. The results showed a significant decrease at (P <0.05) in the weight gain of the rat groups orally administered with Bisphenol A at 10, 20 mg/kg concentrations, as it caused a significant decrease in the weight gain (- 4.7, - 7.23) g respectively compared to the control group that was 36.4 g. There was a significant effect of adding aloe vera gel at 20 % concentration in reducing the effect of Bisphenol A on the body weight compared with the control group which positively increases with concentration.

| Groups                  | Weight gain | Final weight | Initial weight |
|-------------------------|-------------|--------------|----------------|
| Control                 | 155.54      | 191.94       | 36.4a          |
| Bisphenol A 10 mg/kg    | 140.28      | 135.58       | - 4.7d         |
| Bisphenol A 20 mg/kg    | 148.74      | 141.51       | - 7.23e        |
| Aloe Vera 20% + Bisphenol A 10 mg/kg | 153.89 | 152.27 | 1.62b |
| Aloe Vera 20% + Bisphenol A 20 mg/kg | 151.12 | 148.58 | 2.54c |

*Different letters in one column indicate significant differences at a 0.05 probability level.

The results were in agreement with [27] as they reported a decrease in the weight of rats when Bisphenol A was added to its drinking water. The results agreed also with [16] who found that there was a decrease in the weight of rats in all groups of rats fed on food contaminated with Bisphenol A. [28] reported that Aloe vera increased the body weight gain (BWG) in a protected group with different ratios of Aloe vera suspension gel compared to the control group.

Decreased body weight in laboratory animals fed with BPA compounds may be associated with the toxicity of these compounds affecting the growth of animals [29]. This negative effect could be reduced by adding aloe vera gel extract which is binding with BPA compounds in the intestinal area and improves digestive function and prevents its absorption in the intestine, thus reducing the risk of exposure to these compounds [30]. The significant improvement in body weight when using aloe vera extract may be due to the positive effect on the nature of the intestinal flora of the small intestines. The improvement in the rate of live body weight may be due to the ability of the aloe vera plant to improve digestion efficiency due to its enzymes content s that help to break down food, sugars, and fats such as carboxy-peptidase, catalase, cellulase, and peroxidase, moreover, this plant contains many vitamins such as vitamins (A, C and E), group B vitamins, folic acid, and choline. B group vitamins are involved in the metabolism of amino acids [31].

3.2. The effect of Alo Vera on kidney function

Table 2 indicates the effect of adding Bisphenol A to a rat’s drinking water at a concentration of (10, 20) mg/kg for 28 days on its kidney functions. The results showed a significant increase in the values of urea, creatinine, and uric acid in treatments of adding Bisphenol A at 10, 20 mg/kg concentrations, as it reached (30, 37) (1.68, 1.84) and (2.61, 2.96) mg / DL, respectively, compared with the control group that was (24, 0.71 and 2.02), mg / DL. There was a significant effect of adding 20 % of aloe vera gel in reducing the negative effect of Bisphenol A on the values of urea, creatinine, and uric acid compared to the control group which is positively correlated with its concentration.
Table 2. Effect of aloe vera gel on kidney function in female rats exposed to Bisphenol A after a period of 28 days.

| Groups                        | Urea   | Creatinine | Uric acid |
|-------------------------------|--------|------------|-----------|
| Control                       | 24e    | 0.71e      | 2.02e     |
| Bisphenol A 10 mg/kg          | 30b    | 1.68c      | 2.61c     |
| Bisphenol A 20 mg/kg          | 37a    | 1.84a      | 2.96a     |
| Aloe Vera 20% + Bisphenol A 10 mg/kg | 26d    | 1.47d      | 2.24d     |
| Aloe Vera 20% + Bisphenol A 20 mg/kg | 29c    | 1.69b      | 2.73b     |

*Different letters in one column indicate significant differences at a 0.05 probability level

The results were in agreement with [32] who found that the level of uric acid increased when rats fed a diet containing 5 and 10 mg/kg/day of BPA compared to the control group. [33] reported that oral administration of BPA has also aroused interest in the nephrological community, as it has been linked to kidney and endocrine disorders, since BPA is cleared by the kidneys, plasma and tissue levels of BPA are markedly increased in patients with impaired renal function. The increased protein catabolism and withdrawal of the amino group from the amino acids explains the high level of urea and these toxic compounds increase blood urea [34]. The increase in uric acid may be attributed to the breakdown of purines or the inability of the kidneys to excrete it, and elevated creatinine in the blood serum is associated with abnormal filtration of molecules by the kidneys [35]. [28] found that the ability of Aloe vera in different ratios to decrease the mean values of uric acid, urea, and creatinine in all tested groups was noticed compared to the control group. The ability of Aloe Vera to reduce the negative impact of animal exposure to BPA is through its ability to bind with these compounds and remove them from the intestine [36]. Oxidative stress is a state of imbalance between oxidants and antioxidants in favor of oxidants causing significant cellular damage [37]. Free radicals play an important role in cellular damage resulting from the use of toxic chemicals, which can lead to cell death [38]. In addition to the development of many diseases [39].

3.3. The effect of Alo Vera on Enzymatic parameters

The effect of Bisphenol A at a concentration of (10, 20) mg / kg on the activity of enzymes in female rats is shown in Table 3. The results showed a significant increase (P <0.05) in the values of ALP, AST and ALT enzymes when treated with Bisphenol A at 10 and 20 mg / kg reaching (145, 157) (55, 62) and (42, 51) IU/ liter respectively compared with the control group which were (136, 42 and 25) IU/ liter respectively. The results also showed a significant decrease in the enzyme’s activity values when adding 20 % of aloe vera gel with Bisphenol A compared with Bisphenol A alone.

Table 3. Effect of aloe vera gel on some enzyme parameters (IU / L) in female rats exposed to Bisphenol A after a period of 28 days.

| Groups                        | ALP   | AST  | ALT  |
|-------------------------------|-------|------|------|
| Control                       | 136e  | 42e  | 25e  |
| Bisphenol A 10 mg/kg          | 145e  | 55e  | 42e  |
| Bisphenol A 20 mg/kg          | 157a  | 62a  | 51a  |
| Aloe Vera 20% + Bisphenol A 10 mg/kg | 141d  | 50d  | 38d  |
| Aloe Vera 20% + Bisphenol A 20 mg/kg | 148b  | 57b  | 47b  |

*Different letters in one column indicate significant differences at a 0.05 probability level

Our results were agreed with [32] who reported that a significant increase in the level of liver enzymes ALT and AST occurred when rats were fed a diet containing 5 and 10 mg/kg/day of Bisphenol A compared to the control group. The results were also in agreement with [40] who found that there was an increase in the activity of the enzyme ALT and AST in rats fed with BPA at a concentration of 25 mg/kg. The results indicated that low concentrations of BPA had no significant effect and causes damage to the liver cells and the exit of enzymes outside the cells into the blood on liver tissue and enzymes, but its increased concentration can cause damage to liver tissue and increase the serum levels of liver enzymes [17]. The reduction in the level of glutathione may be due to the occurrence of oxidative stress caused by continuous treatment of bisphenol A, GSH has active participation in
preventing oxidative stress either through direct removal of free radicals or by the enzymes such as glutathione peroxidase [41].

[28] reported that feeding rats on different ratios of Aloe vera gel decreased serum AST and ALT enzymes compared to the control group and subsequently reduce their toxic effect. The gel of the aloe vera plant prevents the oxidation of fats in the body that the aloe vera plant possesses, which led to an increase in the production of steroid hormones that are the nucleus of sterols in its manufacture, the ability of aloe vera to reduce the negative effect of BPA is through its ability to bind to these compounds and reduce their absorption by the intestine, in addition to the possibility of blocking their association with the villi of the intestine, thus reducing their absorption and subsequently their toxic effect [36,42].

Conclusion

The current study represents for evaluate the effect of oral administration of Aloe vera gel on some biological parameters in laboratory rats that exposed to Bisphenol-A. The results show to the Aloe vera gel reducing the effect of Bisphenol A on the body weight, kidney function (urea, creatinine and uric acid) and Liver enzymes compared with the control group which positively increases with concentration.

References

1. Michel J., Abd Rani N. Z. and Hasain K. (2020) A Review on the Potential Use of Medicinal Plants From Asteraceae and Lamiaceae Plant Family in Cardiovascular Diseases. Front. Pharmacol. 11:852. doi: 10.3389/fphar.2020.00852.

2. Nahar T., Borhan U., Shahdat H., Abdul M. S., and Sohel A. (2013) Aloe vera gel protects liver from oxidative stress-induced damage in experimental rat model. Complement Integr. Med. 10(1): 1–7. doi: 10.1515/cim-2012-0020.

3. Adegbola P, Ilewumi A., Wasu H. and Tolulope O. (2017) Antioxidant and anti-inflammatory medicinal plants have potential role in the treatment of cardiovascular disease: a review. Ann. J. Cardiovasc. Dis., 7(2):19–32.

4. Reynolds, T. and Dweck A. C. (1999) Aloe vera leaf gel: a review update. J. Ethnopharmacol., 68, 3-37DOI: 10.1016/S0378-8749(99)00085-9.

5. Kalimuthu and Vijayakumar S. (2010). Micro propagation of Aloe vera Linn.A Medicinal Plant International Journal of Biotechnology and Biochemistry. 6: 405–410.

6. Mukesh S. S. and Patil M. B. (2010) Aloe vera: Plant of Immortality. International Journal of Pharma Sciences and Research,1(1):7-10.

7. Heyne K. (1987) Tumbuhan Berguna Indonesia. Jilid1. Badan Litbang Kehutanan (Penterjemah), Yayasan Sarana Wana Jaya. Jakarta.

8. Quispe C., Michael V., Jorge B., and Mario S. (2018) Chemical Composition and Antioxidant Activity of Aloe vera from the Pica Oasis (Tarapaca’, Chile) by UHPLC-Q/Orbitrap/MS/MS. Journal of Chemistry, pp 1 – 12.

9. Adzitey F., Anthony A. A. and Udoji J. U. (2019) Antibacterial Effect of Aloe Vera Gel Extract on Escherichia coli and Salmonella enterica isolated from the Gastrointestinal Tract of Guinea Fowls. World Vet J., 9(3): 166–173.

10. AYELOJA Ayodeji Ahmed. (2020). GLIMPSE OF FISH AS PERISHABLE STAPLE. Al-Qadisiyah Journal For Agriculture Sciences, 10(2), 349-375.

11. Jeyasakthy S., Rosdan S., Irfan M. and Azian H. (2017) Antifungal Effect of Malaysian Aloe vera Leaf Extract on Selected Fungal Species of Pathogenic Oomycotysis Species in In Vitro Culture Medium. Oman Medical Journal, 32(1): 41–46.

12. Faheem M., Khalig S. and Lone K. P. (2019) Effect of Bisphenol-A on serum biochemistry and Liver Function in the Freshwater Fish, Catla catla. Pak Vet J. pp. 1 – 5. doi.org/10.29261/pakvetj/2019.003.

13. Adeyi A. A. and Babafemi A. B. (2019) Bisphenol-A (BPA) in Foods commonly consumed in Southwest Nigeria and its Human Health Risk. Scientific Reports, 9:17458. doi.org/10.1038/s41598-019-53790-2.

14. Talsness C. E., Andrade A. J., Kurityama S. N., Taylor J. A. and Vom Saal F. S. (2009) "Components of plastic: experimental studies in animals and relevance for human health". Philos Trans R Soc Lond B Biol Sci. 364(1526): 2079–96. DOI:10.1098/rstb.2008.0281.

15. Ehrlich S., Williams P., Misser S. and Flaws J. (2012) "Urinary Bisphenol A concentrations and early reproductive health outcomes among women undergoing IVF". Hum Reprod. 27(12): 3583–92. DOI:10.1093/humrep/des328.

16. Kobroook A., Wachirasek P., Nipon C. , and Orawan W. (2018) Damaging Effects of Bisphenol A on the Kidney and the Protection by Melatonin: Emerging Evidences from In Vivo and In Vitro Studies. Oxidative Medicine and Cellular Longevity. Vol. 2018:1 – 15.

17. Rahimi O., Farah F., Seyed M. and Banan K. (2016) The Effect of Bisphenol A on Liver Tissue Structure and Liver Enzymes. Qom University of Medical Sciences Journal. 9(12): 1-8.

18. Quispe C., Michael V., Jorge B., and Mario S. (2018) Chemical Composition and Antioxidant Activity of Aloe vera from the Pica Oasis (Tarapaca’, Chile) by UHPLC-Q/Orbitrap/MS/MS. Journal of Chemistry, pp 1 – 12.

19. Kahroob A., Wachirasek P., Nipon C. , and Orawan W. (2018) Damaging Effects of Bisphenol A on the Kidney and the Protection by Melatonin: Emerging Evidences from In Vivo and In Vitro Studies. Oxidative Medicine and Cellular Longevity. Vol. 2018:1 – 15.

20. Durrani F. R., Sana U., Chand N., Durrani S. and Akhtar S. (2008) Using aqueous extract of aloe gel as anticoccidial and immune stimulant agent in broiler production. Sarhad J. Agric., 24(4): 665-670.
[21] Lawrence R., Tripathi P. and Jeyakumar E. (2009) Isolation purification and evaluation of antibacterial agents from Aloe vera. Brazilian Journal of Microbiology. 40: 906-915
[22] National Research Council Recommended (NAS-NRC) (2002) Dietary Allowance. 15th ed. Washington, DC. National Academy Press.
[23] Sorg D. A. and Buckner B. (1964) A simple method of obtaining venous blood from small laboratory animals. Proc. Soc. Exp. Bio. Med., 115: 1131.
[24] Tietz Y. (2005) Clinical Biochemistry, 6th ed., McGraw-Hill, New York, p. 825
[25] SAS. SAS/STAT. User's Guide for Personal Computers Institute. USA: Cary Inc; 2010. doi.org/10.1007/s00362-008-0156-x.
[26] Duncan D. (1955) Multiple range and Multiple F-Test. Biometrics. 11:1-42
[27] Mohammed J. M., Karkaz M. T. and Amin S. B. (2015) The Effectiveness of Two Species of Lactic Acid Bacteria Lactobacillus casei and Lb. acidophilus in Some Biological Parameters of Rats Exposed to the Bisphenol-A. Tikrit Journal for Agricultural Sciences.15(2): 34-44.
[28] Ismael S. M., Al-Sayed H. M. A., Abdelrahman R. A. and Marwa F. M. (2018) Protective effect of Aloe vera gel extract plant on liver diseases of experimental rats. African J. Biol. Sci., 14 (1): 61-77.
[29] Mohammed, M.A., Abdulridha, W.M., Abd, A.N. (2018). Thickness effect on some physical properties of the Ag thin films prepared by thermal evaporation technique. Journal of Global Pharma Technology, 10(3), 613-619.
[30] Durabghane B. and Samuel N. N. (2014) A review on effects of Aloe vera as a feed additive in broiler chicken diets. Ann. Anim. Sci., 14(3): 491–500. DOI: 10.2478/aas-2014-0026.
[31] Gupta A. and Swati R. (2017) Clinical importance of aloe vera: Review. Research J. Topical and Cosmetic Sci. 8(1): 30-39.
[32] Mourad I. M. and Khadrawy Y. A. (2012) The Sensitivity of liver, kidney and testis of rats to oxidative stress induced by different doses of Bisphenol A, Inter. J. of Life Science and Pharma Research 2(2):19-28.
[33] Mas S., Jesús E. and González-Parra E. (2017) The importance of bisphenol A, an uraemic toxin from exogenous sources, in haemodialysis patients. Nefrologia 37(3): 229-356. DOI: 10.1016/j.nefroe.2017.06.004
[34] Varely H. (1987) Practical clinical biochemistry. 6th ed. Eds. Gowenlock AH, McMurray JR & Mclauchlan DM. London, Heinemann Medical Books. pp. 477-549.
[35] Bansal A. K., Bansal M., Soni J. and Bhattachar D. (2005) Protective role of Vitamin E pre-treated on N-nitrosodiethylamine -induced oxidative stress in rat liver. Chemnico-Biological Interactions 156: 101-111
[36] Mohammed, M.A. (2020). Structural, Optical , Electrical and Gas Sensor Properties of ZrO2 Thin Films prepared by Sol-Gel Technique. Neuroquantology, 18(3), 22-27. DOI:10.14704/nq.2020.18.3.nq20146
[37] Jurank J. and Bezek S. (2005) "Controversy of the free radical hypothesis: reactive oxygen species – causes or consequence of this tissue injury – gen". Physiol. Biophysiol. 24(3): 263-278.
[38] Delattre J., Beaudoux J. and Bonne D. "Radicaux liberset stress oxidant". Aspects Bio. Pathol. 2005; (9): 355-379.
[39] Aitken R. L. and Bakar M. A. "Oxidative stress and male reproductive biology", Vertebrate Rep. Sci. Technol. 2004; 16(5): 581-588. DOI:10.10371/RD03089.
[40] Korkmaz A., Aydogan M., Kolankaya D. and Barlas N (2010) Influence of vitamin C on bisphenol A, nonylphenol and octyl -phenol induced oxidative damages in liver of male rats. Food and Chem. Toxico., 48: 2865- 2871.
[41] Suleyman D., Mustafa Y., Michmet K., Natan A., Divler A. and Ahmet A. (2003) "Role of free radicals in peptic ulcer and gastritis". Turk. J. Gastroenterol. 14(1): 39-43.
[42] Hussein R. M. and Eid J. I. (2013) Pathological mechanisms of liver injury caused by oral administration of bisphenol A. Life Science Journal, 10(1): 663-673.