The Therapeutic role of Moringa Oleifera Against Bisphenol A toxicity That Induce Renal Effects in Rats

Hind Mohammed Saleh¹, Hani Sabbar Ayed¹ and Ahmed Ibrahim Salih²

¹Dep. of Food Scienceand Biotechnology, College of Agriculture, Tikrit University, Iraq.
²Dep. of Mechanization and Agricultural Equipments, College of Agriculture, University of Kirkuk, Iraq.

Email: hindmohammed@tu.edu.iq

Abstract

The objective of the current work was to induce histological lesions by BPA(Bisphenol A)and then diagnosis the therapeutic role of Moringa oleifera. 66 adult male rats were used in the present work and divided as following: Rats were administrated (orally) normal saline as control group. Rats group were administrated (orally) 5mg BPA and divided into 4 subgroups were each subgroup treated with Moringa oleifera (100mg/kg, 200mg/kg, 300mg/kg and 400mg/kg), respectively. Rats were administrated (orally) 10mg BPA and divided to 4 subgroups were each subgroup treated with Moringa oleifera (100mg/kg, 200mg/kg, 300mg/kg and 400mg/kg), respectively. The findings of BPA groups showed significant (P≤0.05) elevated in urea and creatinine with different histological lesions in the kidney include damaged glomerulus, degeneration of tubules cells, and lymphocytes infiltration. After treatment with Moringa oleifera, renal parameters and kidney tissues were back to the normal state and non-significant (P≤0.05) changes compared with the control group.

Keywords: Bisphenol A, Urea, Moringa oleifera, Kidney tissue.

1. Introduction

*Moringa oleifera* is a kind of local medicinal Indian plant [1]. *M. oleifera* is rich in nutrition owing to the presence of a variety of essential chemical materials present in its different parts. *M. oleifera* contains 7 times vitamin C more than oranges, and 10 times vitamin A compare to carrots, 17 times calcium compared to milk, 9 times protein compare to yogurt, and 15 times potassium compare to bananas [2-4]. The leaves define as the most nutritious part of *M. oleifera*, being an important source of vitamins (B complex, C, K, and A) manganese, and proteins [5]. Some ions of calcium in the leaves of *Moringa* are bound like oxalate crystals [6-7]. The research and studies have referred to the positive effect of *M. oleifera* on blood lipid profiles and secretion of insulin [8]. The leaves extracts contain different kinds of polyphenols [9]. *Moringa* extracts were exhibited antioxidant activities and anticancer agents. The leaves compounds, which are responsible for the anticancer activities, include glucosinolates, benzyl isothiocyanate, and niazimicin [10-11]. Bisphenol-A (BPA) is defined as one of the most significantchemicals introduced essentially in plastics made of polycarbonate and in epoxy resins, BPA is also widely utilized in manufacturing cans of food and drink [12-13]. Various studies referred that BPA leads to adverse effects on the tissues of the brain, reproductive system [14], liver tissues, and other tissues [15]. Therefore, the present study aimed to induce histological changes by BPA and then finding the therapeutic role of *M. oleifera*.

2. Materials and Methods

2.1. Animal model

66 adult male rats, (wt:160-200mg) obtained from Agriculture College, Tikrit University, Iraq.

2.2. *Moringa oleifera* leaf meal

The experiment was performed to replace the soybean meal with (MOLM) *Moringa oleifera* leaf meal in the formulated diet of adult male rats.
2.3. Experimental design

66 adult male rats were utilized in the present work as following groups (6 in each studied group):

- Rats were administrated (orally) 1ml of normal saline (as a control group).
- Rats were administrated (orally) 5mg/kg BPA (Alpha Chemica, India).
- Rats were administrated (orally) 10mg/kg BPA.
- Rats were administrated (orally) 5mg BPA and treated with 100mg/kg.
- Rats were administrated (orally) 5mg BPA and treated with 200mg/kg.
- Rats were administrated (orally) 10mg BPA and treated with 300mg/kg.
- Rats were administrated (orally) 10mg BPA and treated with 400mg/kg.
- Rats were administrated (orally) 5mg BPA and treated with 100mg/kg.
- Rats were administrated (orally) 5mg BPA and treated with 200mg/kg.
- Rats were administrated (orally) 10mg BPA and treated with 300mg/kg.
- Rats were administrated (orally) 10mg BPA and treated with 400mg/kg.

2.4. Renal parameters assay

Urea and creatinine were determined by using the reagent kits (fuji film device with urea and creatinine, France).

2.5. Histological Study

Rats were killed by cervical dislocation. Immediately after death, the kidney was removed then fixed in 10% formalin until the preparation for the histological section. The preparation of slides for kidneys and stained by Routine stain (Hematoxyline and Eosin stains) [16].

2.6. Statistical Analysis

The renal parameters analysis was done by utilizing one-way ANOVA. The renal parameters were expressed as mean ± SD. The statistical significance was set at levels P≤ 0.05 [17].

3. Results

3.1. Urea and creatinine levels

Urea levels showed significant differences (P≤0.05) in Bisphenol A (5mg & 10mg) groups compared to the control group. After treatment with Moringa oleifera leaf meal, urea levels back to normal range and non-significant (P≤0.05) differences were noticed compared with the control group (Figure 1). Creatinine levels increased significantly (P≤0.05) in Bisphenol A (5mg & 10mg) groups compared with the control group. After treatment with *M. oleifera*, creatinine levels back to normal range and non-significant (P≤0.05) differences were showed compared with the control group (Figure 2).

![Figure 1. Levels of urea studied groups.](image-url)
3.2. Histological study

In the control group, figure (3), showed anormal structure of the glomerulus that is surrounded by Bowman's capsule, convoluted tubule (proximal and distal tubules). Figure (4) showed a damaged glomerulus, thickening wall of blood vessels with congestion, lymphocytes infiltration with a hyaline cast in Bisphenol A groups (5mg). After treatment with the M. oleifera, a group of 5mg Bisphenol A with 100mg M. oleifera showed damage glomerulus and thickening wall of blood vessels with lymphocytes infiltration (Figure5). However, the Bisphenol A group treated with 200mg (figure6), 300mg (figure7), and 400mg (figure8) M. oleifera, repair the kidney tissue back to normal state. Figure (9) showed damaged glomerulus, thickening wall of blood vessels with congestion, and lymphocytes infiltration with the hyaline cast in Bisphenol A group (10mg). After treatment, a group of 10mg Bisphenol A with 100mg M. oleifera showed damage glomerulus and thickening wall of blood vessels with lymphocytes infiltration (figure 10). But, Bisphenol A and treated with 200mg (figure 11), 300mg (figure 12), and 400mg (figure 3) M. oleifera showed the kidney tissue back to normal state.
Figure 5. Kidney of 5mg Bis & 100mg MOLM group show damage glomerulus (DG), degeneration (D) cells of tubules, thickening wall (TW) of blood vessels, lymphocytes infiltration (LI) and fibrocytes (F) H&E X400.

Figure 6. Kidney of 5mg Bis & 200mg MOLM group show normal structure of glomerulus (G), Bowman's capsule (BC), distal tubules (DT) and proximal tubules (PT) H&E X400.

Figure 7. Kidney of 5mg Bis & 300mg MOLM group show glomerulus (G), Bowman's capsule (BC), distal tubules (DT) and proximal tubules (PT) H&E X400.

Figure 8. Kidney of 5mg Bis & 400mg MOLM group show glomerulus (G), Bowman's capsule (BC), distal tubules (DT) and proximal tubules (PT) H&E X400.
Figure 9. Kidney of 10mg Bis group show damage glomerulus (DG), thickening wall (TW) of blood vessels, fibrocytes (F) and lymphocytes infiltration (LI) H&E X400.

Figure 10. Kidney of 10mg Bis & 100mg MOLM group show damage glomerulus (DG), degeneration (D) and slough (SE) epithelial cells of tubules and lymphocytes infiltration (LI) H&E X400.

Figure 11. Kidney of 10mg Bis & 200mg MOLM group show damage glomerulus (DG), thickening wall (TW) of blood vessels with congestion (CON) and lymphocytes infiltration (LI) H&E X400.

Figure 12. Kidney of 10mg Bis & 300mg MOLM group show of glomerulus (G), Bowman's capsule (BC), distal tubules (DT) and proximal tubules (PT) H&E X400.
4. Discussion

The current results of kidney functions parameters and tissues showed significant differences (P≤0.05). Kidney functions parameters showed significant elevation (P≤0.05) in groups of Bisphenol A (5mg & 10mg) compared with the control group. The current findings agree with [18] who referred that the exposure to Bisphenol for 5 weeks lead to azotemia, as shown by elevated urea and creatinine levels. These results reflect that BPA harms the tissue of the kidney and leads to disorders of renal functions. The current results are related to the previous work showing BPA-induced proteinuria and podocytopathy in mice [19]. About the role of M. oleifera extract, the current study show improvement of kidney functions and tissue. In recent studies, it was demonstrated that the water extract of leaves of M. oleifera posses polyphenols and antioxidant activity [20]. Also, there are several studies referred that to the leaves of M. oleifera had been polyphenols and flavonoid compounds and possess antioxidant activity [21, 22]. This might explain the role of M. oleifera as an antioxidant, which caused improvement in kidney function and tissues and back to normal state after treatment. Otherwise, the quercetin may have been participated in the decreasing of the inflammatory process by inhibiting the activity of the neutral factor kappa-beta (NF-kβ) and NF-kB-dependent events and the inflammation [23].

References

[1] Abdull Razis, A. F.; Muhammad D. I. and Saie B. K. (2014). Health benefits of Moringa oleifera. Asian Pac J Cancer Prev, 15 (20), 8571–8576.
[2] Rockwood J.L.; Anderson B.G. and Casamatta, D.A. (2013). Potential uses of Moringa oleifera and an examination of antibiotic efficacy conferred by M. oleifera seed and leaf extracts using crude extraction techniques available to underserved indigenous populations, Int. J. Phytotherpy Res. 3: 61–71.
[3] Kasolo, J.N.; Bimenya G.S.; Ojok L. and Ochieng J. (2010). Phytochemicals and uses of Moringa oleifera leaves in Ugandan rural communities, J. Med. Plants Res. 4: 753–757.
[4] Gopalakrishnan L.;, Kruthi D. and Devarai S. K. (2016). Moringa oleifera: A review on nutritive importance and its medicinal application. Food Sci. Human Wel. 5: 49–56.
[5] Peter, K.V. (2008). Underutilized and Underexploited Horticultural Crops., Volume 4. New India Publishing. p. 112.
[6] Freiberger, C. E.; Vanderjagt, D. J.; Pastuszyn, A.; Glew, R. S.; Mounkaila, G.; Millson, M.; Glew, R. H. 1998. Nutrient content of the edible leaves of seven wild plants from Niger. Plant Foods for Hum. Nutr. 53: 57 – 69.
[7] Olson, M. E.; Carlquist, S. (2001). "Stem and root anatomical correlations with life form diversity, ecology, and systematics in Moringa (Moringaceae)". Botanical Journal of the Linnean Society. 135 (4): 315–348.
[8] Cerf, M.E. (2013). Beta cell dysfunction and insulin resistance, Front. Endocrinol. 4: 1–12.
[9] Sreelatha, S. and Padma, P. R. (2009). "Antioxidant activity and total phenolic content of Moringa oleifera leaves in two stages of maturity". Plant Foods for Human Nutrition, 64 (4): 303–311.
[10] Makkar HP, Francis G, Becker K (2007). "Bioactivity of phytochemicals in some lesser-known plants and their effects and potential applications in livestock and aquaculture production systems". Animal. 1 (9): 1371–91.
[11] Asare, GA; Nyarko, A (2012). "Toxicity potentials of the nutraceutical Moringa oleifera at supra-supplementation levels". Journal of Ethnopharmacology, 139 (1): 265–272.
[12] Brotons, J.A.; Olea-Serrano, M.F.; Villalobos, M.; Pedraza, V. and Olea, N. (1995). Xenoestrogens released from lacquer coatings in food cans. Environ Health Perspect., 103: 608–612.
[13] Abid, Q. H. and Ayyed H. H. (2017). Effect of bisphenol-A on reproductive system of female rats (Rattus Norvegicus). J. Kerbala Uni.15(1): 56-62.
[14] LAng, I. A., Galloway, T. S., Scarlett, A., Henley, W. E., Depledge, M., Wallace, R. B. & Melzer, D. 2008. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. JAMA, 300, 1303-10.
[15] Nakagawa, Y. & Tayama, S. 2000. Metabolism and cytotoxicity of bisphenol A and other bisphenols in isolated rat hepatocytes. Arch Toxicol, 74, 99-105.
[16] Saleh, A. H. (2020). Potential Role of Titanium Dioxide (TiO2) Nanoparticles against the Toxicity of Leishmania Tropica in Adult Albino Male Rats. J. Glo.Pharm.Tech.11(3): 453-457.
[17] Saleh, A. H. (2018). The Potential Effect of Grape Seeds Extract against Lead toxicity That Induces Infertility to Male Rats Ahmed Hamad Saleh. Tikrit J. Pur. Sci. 23 (1): 70-74.
[18] Kobroob, 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. Oxid. Med. Cellu. Lon. 2018:1-15.
[19] Olea-Herrero N.; Arenas M. I. and Muñoz-Moreno C. (2014). Bisphenol-A induces podocytopathy with proteinuria in mice. J. Cellu.Phy. 229 (12): 2057–2066.
[20] Charoensin S. and Wongpoomchai R. (2012). Effect of aqueous extract of Moringa oleifera leaves on quinone reductase activity. Naresuan Phayao J. 5(3):101-109.
[21] Luqman S, Srivastava S, Kumar R, Maurya AK, Chanda D (2012). Experimental assessment of Moringa oleifera leaf and fruit for its antistress, antioxidant, and scavenging potential using in vitro and in vivo assays. Evid. Based Complement. Alternat. Med. 2012:1-12.
[22] Santos AF, Argolo AC, Paiva PM, Coelho LC (2012). Antioxidant activity of Moringa oleifera tissue extracts. Phytother. Res. 26(9):1366-1370.
[23] Das, N.; Sikder, K.; Ghosh, S.; Fromenty, B. and Dey, S. (2012). Moringa oleifera Lam. leaf extract prevents early liver injury and restores antioxidant status in mice fed with high-fat diet. Indian J. Exp. Biol. 50: 404–412.