Journal of International Pharmaceutical Research, ISSN: 1674-0440
Available at http://ijprjournals.com/abstractt.php?id=248

Histological effects of Spironolactone drug on heart, lung, liver, kidney, and spleen of male albino mice

Hadeel Kamil Khaleel

1. Histology Dep. Medical Laboratory techniques, AL_Rasheed University College, Baghdad, Iraq.
Correspondence author: HadeelKamilKhaleel, e-mail: hadilbiologist@yahoo.com 07712728305
Received: 08-05-2018, Revised: 21-07-2018, Accepted: 17-09-2018, Published online: 03-12-2018

How to cite this article: HadeelKamilKhaleel (2018) Histological effects of Spironolactone drug on heart, lung, liver, kidney, and spleen of male albino mice, Journal of International Pharmaceutical Research 9(1): 357-362

Abstract

This study was designed to show the histological changes of heart, lung, liver, kidney and spleen in male albino mice which treated by different concentrations (200, 400 and 800 mg\kg) of spironolactone have been investigated. Twenty adult male mice were divided into four groups, with five male per group. Three concentration of spironolactone were applied to the respective groups (other than the control), 200mg/kg, 400mg/kg and 800mg/kg. The animals were given 0.1 ml per 10 gm body weight per concentration of spironolactone once a day during two weeks. The control group animals were given distilled water. The organ specimens were obtained from mice treated with spironolactone and processed to evaluate the histological changes. The present study has shown several histopathological changes in heart of the treated mice with the drug represented by shrinkage and necrosis of wide spread area of muscle fiber. In the lung, the drug caused chronic inflammatory cells infiltration around the bronchioles and slight emphysematous changes. In addition there were depleting of glycoprotein granules, dispersed apoptotic of hepatocytes and inflammatory cells infiltration in the liver tissue. At the high dose the drug caused chronic inflammatory cells infiltration, necrosis of renal tubules and congestion in the kidney tissue. In the spleen, the drug caused slight widening of white pulp with beginning formation of germinal center and reduction of red pulp. The histological changes induced in the organs by spironolactone could be a mistake in the use of this drug.

Key words: Histological effects, spironolactone, male albino mice.

Introduction

Spironolactone is a steroidal drug, administered as a diuretic that stimulates potassium to treat high blood pressure [8]. The drug has also used for the treatment of hypokalemia, edema in congestive heart failure, ascites and essential hypertension [4, 12]. The chemical structure of spironolactone is a lipophilic drug, crystalline powder, insoluble in water; it is soluble alcohol and ethyl acetate, very soluble in chloroform, and benzene and in methanol [5]. Spironolactone is a competitive anti-aldosterone that works in distant isolated renal tubules to increase sodium, and water secretion and reduce potassium elimination [13].Prevention of cardiovascular disease is essential in chronic dialysis patients. Recently, a low dose of spironolactone has been shown to lower cardiovascular mortality in patients with acute heart failure. However, since dialysis patients are susceptible to hyperkalemia, a known side effect of spironolactone, this treatment is not used in this population [14]. We performed a study to investigate the histological changes in the heart, lung, liver, kidney and spleen of the male albino mice treated by spironolactone drug.

Methods

Healthy white albino male mice weighing between 25-30g were kept in separate plastic cages under controlled conditions of temperature and light, fed ad-libitum and used for scientific research in the laboratories of Biotechnology Research Center\ Al-Nahrain University.

The animals were divided into four groups, five animals in each. The first group was control treated with normal saline.

The other groups were treated daily for two weeks with 200, 400, 800 mg/kg of body weight oral administration of spironolactone drug, respectively for two weeks. At the end, the animals were anaesthetized with chloroform. After dissection of the abdomen, the heart, lung, liver, kidney and spleen were removed and fixed in formaline for 24 hours, dehydrated in alcohol, cleared in xylene and embedded in paraffin wax. The blocks obtained were section and stained by hematoxylin and eosin stain (H&E) [7].

Results

Results of the present study revealed the following:

Heart

A study has demonstrated that the oral administration in male mice of spironolactone at a concentration of 200 mg\kg for two weeks caused

shrinkage and necrosis of wide spread area of muscle fiber (Fig. 2). Oral administration of 400 and 800 mg\kg of spironolactone showed necrosis of wide spread area of muscle fiber (Fig. 3, 4) compared to the control group (Fig. 1)

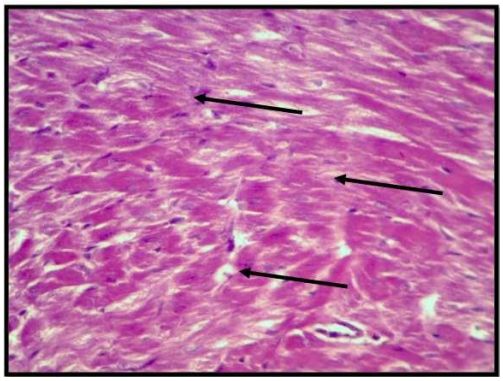

Figure-1: Light photomicrograph of heart tissue in a control mice showing normal architecture of cardiac muscle fibers (arrows) 400X, H&E.

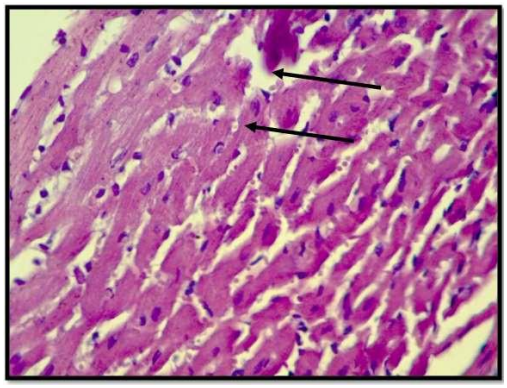

Figure-2:Light photomicrograph of heart tissue in 200mg\kg of spironolactone treated mice showing shrinkage and necrosis of wide spread area of muscle fiber (arrow) 400X, H&E.

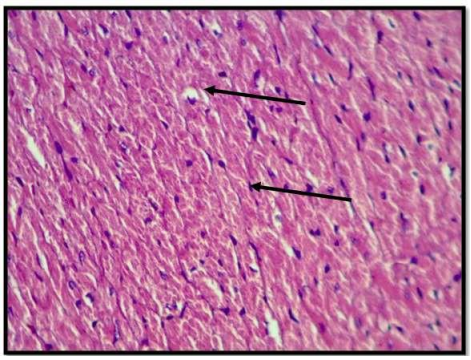

Figure-3: Light photomicrograph of heart tissue in 400mg\kg of spironolactone treated mice showing necrosis of wide spread area of muscle fiber (arrow) 400X, H&E.

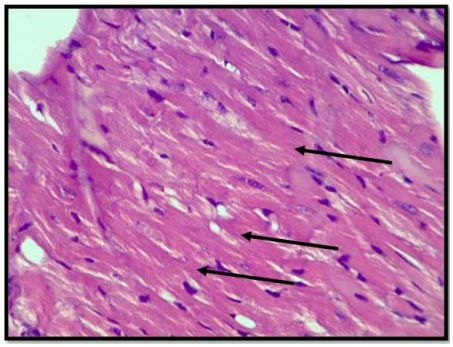

Figure-4: Light photomicrograph of heart tissue in 800mg\kg of spironolactone treated mice showing dispersed necrosis of cardiac muscle fiber (arrow) 400X, H&E.

Lung

Histological examination of mice lung treated with the 200, 400 and 800 mg\kg of spironolactone, respectively showed that there were mild chronic inflammatory cells infiltration around the bronchioles and slight emphysematous changes (Fig. 6, 7, 8) compared to control group (Fig. 5).

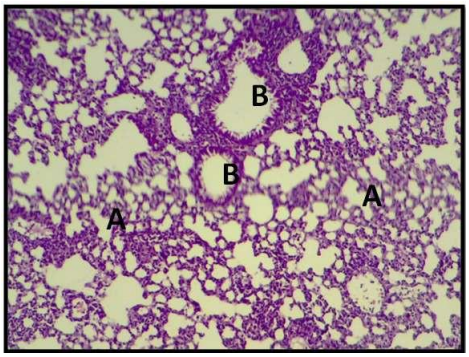

Figure-5: Light photomicrograph of lung tissue in control mice showing normal respiratory bronchioles (B) and alveoli (A) 100X, H&E.

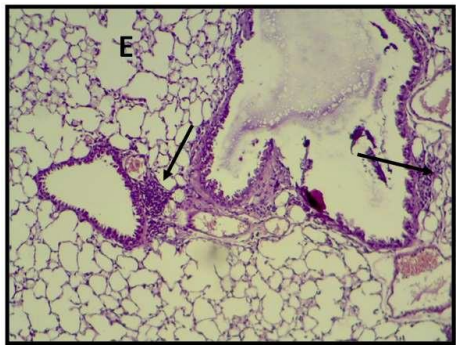

Figure-6: Light photomicrograph of lung tissue in 200mg\kg of spironolactone treated mice showing mild chronic inflammatory cells infiltration around the bronchioles (arrows) and slight emphysematous changes 100X, H&E.

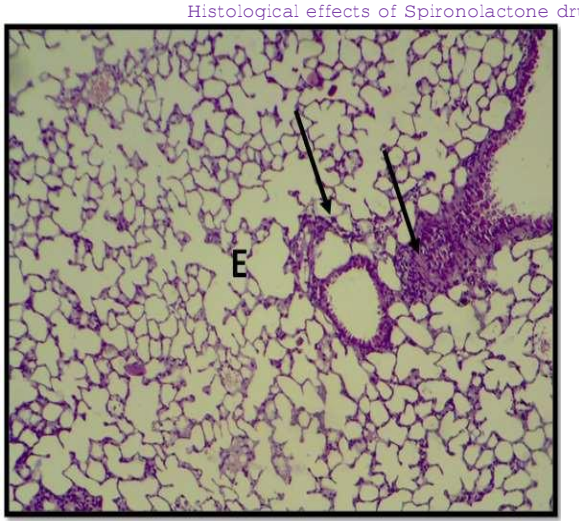

Figure-7: Light photomicrograph of lung tissue in 400mg\kg of spironolactone treated mice showing mild chronic inflammatory cells infiltration around the bronchioles (arrows) and slight emphysematous changes (E) 100X, H&E.

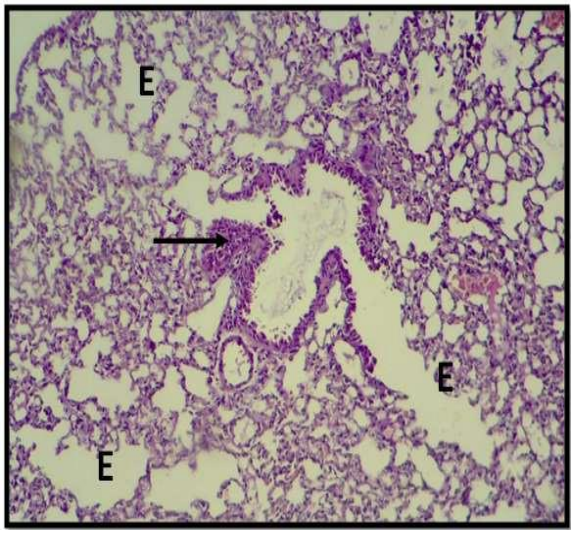

Figure-8: Light photomicrograph of lung tissue in 800mg\kg of spironolactone treated mice showing mild chronic inflammatory cells infiltration around the bronchioles (arrows) and slight emphysematous changes (E) 100X, H&E.

Liver

No histological changes were observed in liver by administration of spironolactone at a dose 200 mg\kg but with depletion of glycoprotein granules (Fig. 10). Male mice received 400 mg\kg of a drug showed deplete of glycoprotein granules with dispersed apoptotic of hepatocytes (Fig. 11). Oral administration of 800 mg\kg of spironolactone showeddeplete of glycoprotein granules with inflammatory cells infiltration (Fig. 12) compared to control group (Fig. 9).

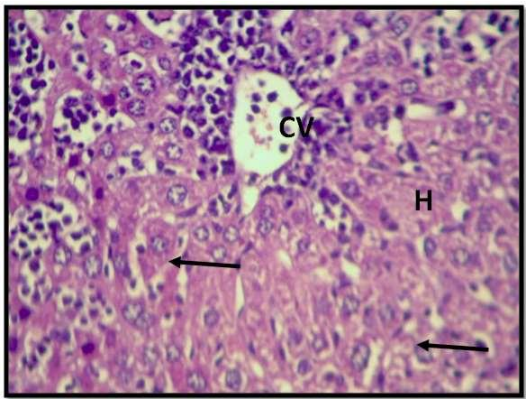

Figure-9: Light photomicrograph of liver tissue in control mice showing hepatocytes (H) radiating from central vein (CV) and sinusoid (arrow) 400X, H&E.

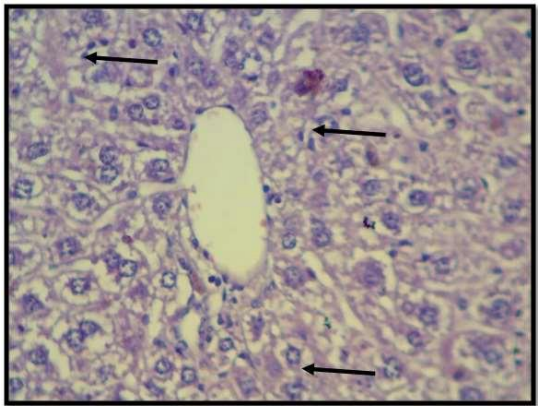

Figure-10: Light photomicrograph of liver tissue in 200mg\kg of spironolactone treated mice showingnormal structure of hepatocyte but withdepletion of glycoprotein granules (arrows) 400X, H&E.

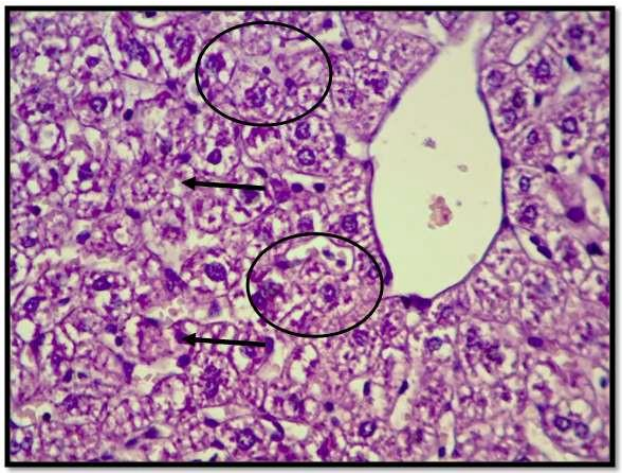

Figure-11: Light photomicrograph of liver tissue in 400mg\kg of spironolactone treated mice showing deplete of glycoprotein granules (arrow) with dispersed apoptotic of hepatocytes (circle) 400X, H&E.

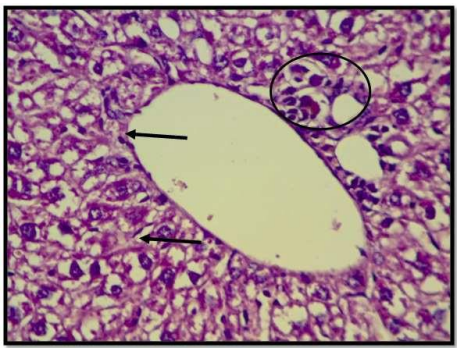

Figure-12: Light photomicrograph of liver tissue in 800mg\kg of spironolactone treated mice showing deplete of glycoprotein granules (arrow) with inflammatory cells infiltration (circle) 400X, H&E.

Kidney

The current study has shown that the oral dose of mice at 200 and 400 mg\kg of spironolactone respectively there were no histological changes in the renal tissue (fig. 14 and 15).When the mice treated with 800 mg\kg of spironolactone showed chronic inflammatory cells infiltration, necrosis of renal tubules and congestion in the kidney tissue (fig.16) compared with control group (fig. 13).

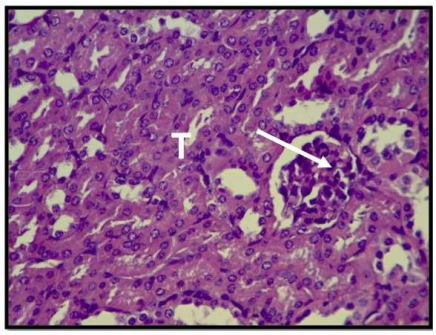

Figure-13: Light photomicrograph of kidney tissue in control mice showing normal glomerulus (arrow), proximal and distal convoluted tubules (T) 400X, H&E.

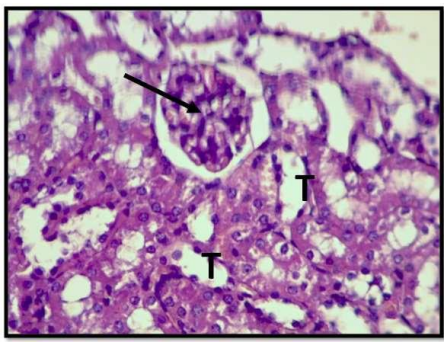

Figure-14:Light photomicrograph of kidney tissue in 200mg\kg of spironolactone treated mice showing normal glomerulus (arrow), normal proximal and distal convoluted tubules (T) 400X, H&E.

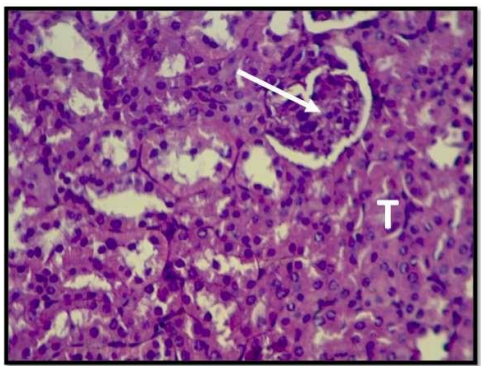

Figure-15: Light photomicrograph of kidney tissue in 400mg\kg of spironolactone treated mice showing normal glomerulus (arrow), normal proximal and distal convoluted tubules (T) 400X, H&E.

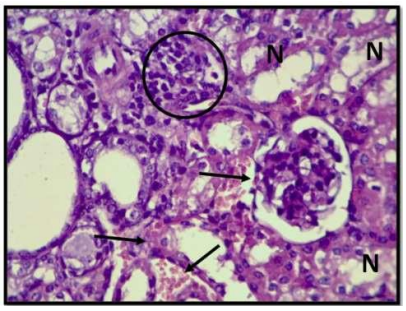

Figure-16: Light photomicrograph of kidney tissue in 800mg\kg of spironolactone treated mice showing chronic inflammatory cells infiltration (circle), necrosis of renal tubules (N), congestion (arrow) 400X, H&E.

Spleen

The current study revealed that spironolactone 200 mg\kg induced widening of white pulp with reduction of red pulp of spleen tissue(fig. 18). Spleen section of treated mice with 400 and 800 mg\kg of spironolactone showed slight widening of white pulp with beginning formation of germinal center and reduction of red pulp (fig. 19 and 20) compared to control group (fig.17).

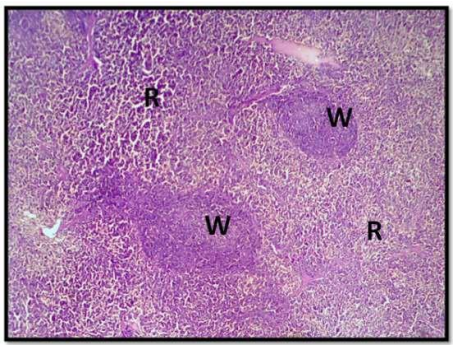

Figure-17: Light photomicrograph of spleen tissue in control mice showing white pulp (w) and red pulp ®100X, H&E.

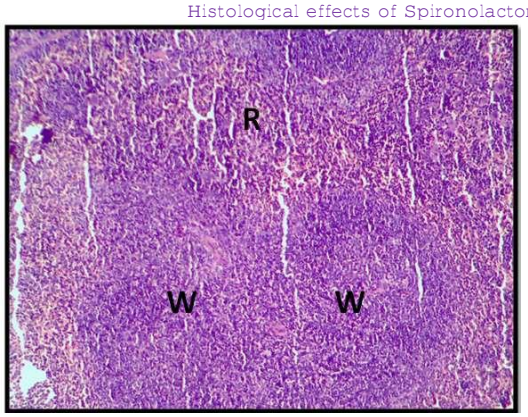

Figure -18:Light photomicrograph of spleen tissue in 200mg\kg of spironolactone treated mice showing widening of white pulp (w) with reduction of red pulp ®100X, H&E.

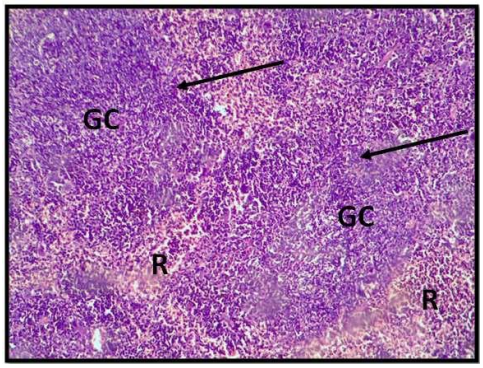

Figure-19: Light photomicrograph of spleen tissue in 400mg\kg of spironolactone treated mice showing slight widening of white pulp (arrow) with beginning formation of germinal center (GC) and reduction of red pulp ®100X, H&E.

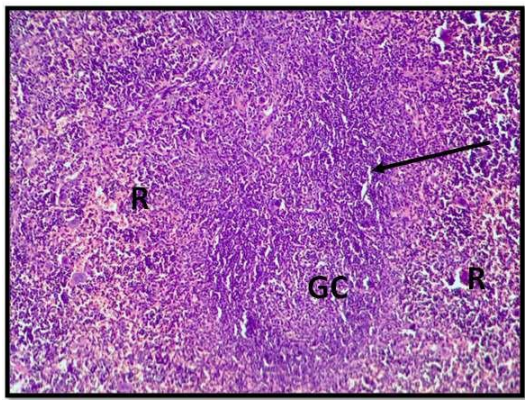

Figure-20: Light photomicrograph of spleen tissue in 800mg\kg of spironolactone treated mice showing widening of white pulp (arrow) with beginning formation of germinal center (GC) and reduction of red pulp ®100X, H&E.

Discussion

Drugs are an important cause of tissue injury. Large number of drugs has been reported to cause tissue injury. In the present study, the histological heart section of treated mice with spironolactone caused shrinkage and necrosis of wide spread area of muscle fiberthese results agree with [11, 2].The lung sections of the treated groups show mild chronic inflammatory cells infiltration around the bronchioles and slight emphysematous similar to researcher [6]. Liver tissue showed no histological changes with the low dose but there are depleting of glycoprotein granules with inflammatory cells infiltration after the animals treated with spironolactone at 400 and 800 mg\kg of body weight [1, 3,and 16]. There were no histological changes in the renal tissue at the low and medium dose but when the mice treated with 800 mg\kg of spironolactone showed necrosis of renal tubules [9, 15], chronic inflammatory cells infiltration and congestion in the kidney tissue [10]. The histopathological changes of the spleen section were widening of white pulp with beginning formation of germinal center and reduction of red pulpthis result was similar to findings by others [17].

Conclusion

This study showed that daily administration with different concentration of spironolactone caused shrinkage and necrosis of heart muscle fiber.There were chronic inflammatory cells infiltration around the lung bronchioles and slight emphysematous changes of. Also, there were depleting of glycoprotein granules, dispersed apoptotic of hepatocytes and inflammatory cells infiltration in the liver tissue. Spironolactone induced chronic inflammatory cells infiltration, necrosis of renal tubules and congestion in the kidney tissue. In the spleen, the drug caused slight widening of white pulp with beginning formation of germinal center and reduction of red pulp. The histological changes induced in the organs by spironolactone could be a mistake in the use of this drug.

References

1. Al-Zahra, J.I.A., Ismael, D.K. and Al-Shawi, N.N. (2017) Preventive effects of different doses of pentoxyfilline against ccl4-induced liver toxicity in rats. Iraqi Journal of Pharmaceutical Sciences: 39-45.
2. Ismail, S.H. and Attyah, A.M. (2012) Protective Effect of Ginger Extract Against Cisplatin-Induced Hepatotoxicity and Cardiotoxicity in Rats. Iraqi Journal of Pharmaceutical Sciences, 21(1): 27-33.
3. Hassan, B.A.W. and Abdullah, S.A. (2016) Some Histological Effects of Panadol Extra on Albino Mice Liver. Journal of Tikrit University For Agriculture Sciences, 16(2): 1-6.
4. British National Formulary (BNF).Cardiovascular system – Heart Failure- Spironolactone. 70th ed. BMJ Group and the Royal Pharmaceutical Society of Great Britain. London. BMA. 2016. https://pharm.reviews/images/statyi/british-national-formulary-2015.pdf.
5. Brandão, F.C., Tagiari, M.P., Silva, M.A.S., Berti, L.F. and Stulzer, H.K. (2008) Physical-chemical

characterization and quality control of spironolactone raw material samples. Pharmaceutical Chemistry Journal, 42(6): 368-376.

6. Hafidh, I., Hani, M. and Rayya, G. (2017) Morphological and Histological Changes in Liver and Lung of mice and Their Administered with Parkizol Drug. Tikrit J Pure Sci.. 22(10): 1-12.
7. Humason, G.L. (1972) Animal tissue technique. 3rd ed. San Francisco: WH. Ferman and Company.
8. Ismail, Y., Chandrasekhar, K.B. and Gunasekaran, V. (2014) A new stability indicating UPLC method development and validation for the simultaneous estimation of metolazone and spironolactone in bulk and in its pharmaceutical formulations. Int. J. Pharm. Pharma. Sci, 6(10): 448-52.
9. HashimZayni, M.M. (2013) Protective Effect of Terfeziaclaveryi Extract on Gentamicin-Induced oxidative stress in Rats. karbala journal of pharmaceutical sciences, 4: 40-50.
10. Mohammed, A. and Zainab, K. (2011) Effect of Diclofenac (Voltaren) in histological structure of kidney in male Rabbits (Oryctolaguscuniculus). Baghdad Sci J.. 8(1): 197-201.
11. Omar, J., Nada, N. and Maha, D. (2012) Possible Cardiac Adverse Effects Induced by Therapeutic Doses of Ciprofloxacin in Juvenile Rats. Iraqi J Pharma Sci. 21(2): 94-97.
12. Rahul, C., Patel, J. and Bapna, M. (2014) Development and validation of analytical method for estimation of Spironolactone in oral suspension. J ChemBiolPhys Sci. 4(3): 2196-2204.
13. Salgado, A., Rosa, M.D.M. and Almeida, A. (2005) Stability of spironolactone in an extemporaneously prepared aqueous suspension: the importance of microbiological quality of compounded paediatric formulations. Eur J Hosp Pharm Sci. 11(3): 68-73.
14. Saudan, P., Mach, F., Perneger, T., Schnetzler, B., Stoermann, C.F., Rossier, M. and Martin, P. (2003) Safety of low-dose spironolactone administration in chronic haemodialysis patients. Nephrol Dial Transplant, 18(11): 2359-2363.
15. Shatha, H., Muntadher, M. and Moayad, M. (2017) Comparative study between the effect of first and second generation of anti-epileptic durgs on hepatorenal toxicity in female albino rats. Kerbala J Pharma Sci. 12: 69-83.
16. Sundus, M. Morphological and Histopathological effect of Dexamethasone on the Embryo of white Mus musculus mice. Diyala J Pure Sci. (2014) July. 10 (3): 103-116.
17. Akharaiyi, Fred Coolborn , Aderoba Adeyemi Adegbemisipo (2018) Medicinal vegetal use by traditional healers in Ekiti State of Nigeria for diabetes treatment. International Journal of Pharmacy Research & Technology, 8 (1), 21-28.