Full Length Research Article
Advancements in Life Sciences – International Quarterly Journal of Biological Sciences

ARTICLE INFO

Date Received: 13/07/2023;
Date Revised: 15/08/2024;
Available Online: 15/10/2024;

Author's Affiliation:
1. College of Veterinary Medicine, Al-Qasim Green University, Al-Qasim – Iraq
2. College of Agriculture and Forestry, University of Mosul – Iraq

***Corresponding Author:**
Mozhir K. K. Almahdawi
Email: mozhir2007@uomosul.edu.iq

How to Cite:
Al-Mousawi ZHK, Almahdawi MKK, Al-Bayati ASS (2024). Impact of varying sorbitol concentrations on hematological and biochemical blood parameters in Wistar rats (*Rattus Norvegicus*). Adv. Life Sci. 11(4): 767-772.

Keywords:
Sorbitol; Hematological parameters; FSH; LH; Wistar rats

Open Access

Impact of varying sorbitol concentrations on hematological and biochemical blood parameters in Wistar rats (*Rattus norvegicus*)

Zahraa H. K. Al-Mousawi[1], Mozhir K. K. Almahdawi[2*], Abdulsatar S. S. Al-Bayati[2]

Abstract

Background: Sorbitol is an artificial sweetener that is very similar to natural sugar, but it is sweeter than natural sugar and lower in calories. Sorbitol is used as an alternative to natural sugar, and it is extracted from regular glucose. It does not have any negative effects on the animals' health, and it is characterized in safe use in many scientific experiments for the diet of humans and animals.

Methods: This study was conducted in the animal house, College of Veterinary Medicine, Al-Qasim Green University for a period of 90 days. Forty rats of the Wistar strain (*Rattus norvegicus*) were randomly distributed into 4 groups, namely the first group (control group) while the second, third and fourth groups were treated with 100, 200 and 300 µg of sorbitol/kg of body weight .The rats were iso in live weight and age at the beginning of the experiment. Blood samples were drawn at the end of the experimental period.

Results: Increase in level dose of sorbitol resulted significant improvement in accounts of red blood cells, white blood cells, and a significant increase in level of hemoglobin, lymphocytes, and monocytes for second, third, and fourth groups compared to the control group. Moreover, the significant improvement in most of the blood parameters was reflected to significant increase in clotting and bleeding time in the second, third and fourth groups of rats compared to the control group. Also, the results showed a significant increase in the levels of FSH, LH, testosterone, Inhibin and MAD hormones for the second, third and fourth groups compared to the control group.

Conclusions: The results of the current study revealed that sorbitol has many benefits in the diet of humans and animals and has an effect on blood indicators, some sex hormones and antioxidants in the body. It is recommended not to consume excessive sorbitol in the diet.

Introduction

Sorbitol or clocitol is one of the types of alcoholic sugars produced from regular glucose sugar which slowly decomposes inside the body and is added into some types of sugar-free cough syrups. Also, it is used as an alternative sweetener to sugar which is added to varieties of sugar-free food products such as gum, sweets, food, ice cream or soft [1] and non-carbonated drinks as it is present in most types of toothpastes. There are other uses for sorbitol in cosmetics, food industries, and some types of medicines [2]. The action of sorbitol on causing diarrhea, this substance stimulates the activity of bowel movement and causes an increase in amounts of water in the large intestine, which leads to facilitating the removal of waste from the intestine, meaning that it is classified as a non-stimulant laxative [3]. Therefore, sorbitol is used either as an oral syrup or as a suppository. Moreover, sorbitol is naturally present in a few microorganisms like *Zymomonas mobilis* and *Candida boidinii* [6, 7], as well as in apples, pears, peaches, apricots, nectarines, and dried fruits like prunes, dates, and raisins. Comparable to solutions of xylitol and erythritol, which contain negative heat and provide a cooling sensation and pleasing taste in the tongue [4], sorbitol has a solubility 20 times greater than mannitol [8] and less calories than sugars. Because it has synergistic effects with other sweeteners, sorbitol can be well-combined with other food components to enhance their flavor and sweetness [9]. It is not, however, digested by oral bacteria, which produce acids when they break down sugars and starches, which can cause tooth decay or erosion of the tooth enamel layer [10] 25% of sorbitol is absorbed while the remainder is digested by bacteria. Sorbitol affects the synthesis of glycogen in the liver and muscles, which causes a spike in blood sugar following nursing in mothers. Because it is fully digested under normal circumstances, absorbed sorbitol can have an impact on blood glucose levels [11,12]. Large doses of sorbitol may cause diarrhea and abdominal pain especially in presence of other pathogens [13]. Although, the sorbitol is consumed in large quantities, it has been found that the bulk of it causes irritation of the colon which leads to malfunction of the digestive system due to its high molecular weight [14]. After receiving sorbitol, individuals with diabetes saw notable increases in blood glucose concentrations [15]. Furthermore, because sorbitol cannot promote pregnancy, it can accumulate intracellularly and cause osmotic stress [16, 17]. As a result, fructose production is more than ten times more powerful than glucose. The renal route can lead to renal losses of 10% [18]. Abukhomra et al., [19] found that groups treated with varying concentrations of sorbitol (50, 100, or 200 mg) per kg body weight of mice showed a significant increase in the values of red blood cells (RBC), the packed red blood cell volume (PCV), the level of hemoglobin (Hb), white blood cells (WBCs), lymphocytes, neutrophils, monocytes, eosinophils, and basophils in comparison to the control group of mice. This investigation sought to ascertain the impact of sorbitol dosages on some biochemical and hematological blood traits of Wistar rats (*Rattus norvegicus*).

Methods

Animals and study design

In the labs of the College of Veterinary Medicine at Al-Qasim Green University, Iraq, forty Wistar rats (*Rattus norvegicus*) were used for this study. These rats were divided into 4 groups with a mean of 10 rats for each group. The 1st group drenched distilled water, considered as a control group, while the 2nd ,3rd and 4th group were drenched with different levels of sorbitol for ninety days period. The second group received an oral sorbitol /kg of body weight of 100 µgm, the third group received an oral sorbitol of 200 µgm and the fourth group received an oral sorbitol of 300 µgm. The primary weight of the Wistar rats were measured by small scales at the initial period of the experiment and at the final period of the experiment. The blood samples were conducted through the cutting of the tail of the rats and collected heparinized tubes for hematological parameters and plain tubes for the biochemical and hormonal parameters.

Hematological examination

Using a hematology analyzer (Mythic 18VET/France) the heparinized blood samples were utilized to measure hematological parameters such as Hemoglobin (Hb), Packed Cell Volume (PCV), Red Blood Cell count (RBC), and White Blood Cell count (WBC). The procedure was performed according to hematology guidebook, while the differential leukocyte count was carried out through staining the blood smears with Giemsa stain and the different parameters were checked properly [20].

Biochemical examination

Serum samples were prepared (40 microliters) for each test in this study to measure the concentration of enzymes of superoxide Dismutase (SOD), malonaldehyde (MAD) and glucose by using special Chinese kits (Salarbio-China).This procedure was carried out according to the procedure was performed to the chemistry guidebook by using chemical analyzer method (IDEXX- Vet, Arachem, USA) in the blood serum samples of Wistar rats in this study.

Hormonal examination

The Hormones examination which as including insulin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), male hormone (testosterone) and inhibin were calculated by using a proprietary commercial China kit for each hormone: Beijing Salarbio Science & Technology Co. Ltd.(www. Salarbio.com) 400 -968- 6088.

Statistical analysis

The experiment was designed according to a compete randomized design (CRD) according to AL-Zubaidy and AL-Falahy [21] and the ready-made statistical program (SAS) was used to analyze the effects of transactions on the studied traits [22]. The significant differences between the means of the traits studied were tested according by Duncan's polynomial test [23].

Results

Through examining the results of the current study (Table 1), we notice a significant increase in the numbers of red blood cells, white blood cells, hemoglobin concentration, and the percentages of lymphocytes and mononuclear cells in the second, third, and fourth treatments in which the rats were dosed with different levels of sorbitol compared to the control treatment free of sorbitol. The rates of red blood cells accounts reached 6.47,7.22, 7.16, 7.78 $\times 10^6$ corpuscles/ µL, white blood cells accounts was 8.35, 9.47,9.86, 10.68$\times 10^3$ cells, Hemoglobin level was 13.32,13.50, 13.82, 14.62gm, Lymphocytes which were 65.56, 66.37, 69.81,71.43%, Monocytes rats were 6.27, 6.47%, 6.90%, 6.97% respectively. Moreover, there was a significant elevation in clotting time and bleeding time for the 2nd ,3rd,4thgroups of rats which were treated with different levels of sorbitol when compared to the control group. The clotting time was reached 36.02,46.76,57.14,77.96 sec. and bleeding time which were 58.56,72.04,85.86,112.11sec respectively. Conversely there was a notable significant reduction in levels of PCV, Neutrophils and ESR for the 2nd ,3rd ,4th groups of rats in comparison of the control group which were dosed different levels of sorbitol. The level of Neutrophils was 22.51,21.19,21.81,20.50%,PCV 41.47,38.29,34.49,33.53% and ESR was 2.39,2.11,1.97, 1.85 mm/hr respectively (table1). As for the final weight of the rats at the end of the experiment, the results confirmed shown in table (2) that final weight of the rats increased significantly with increasing level of sorbitol dosage in the second, third and fourth experimental treatments compared to the first treatment without sorbitol dosage. The final weight rates of the rats reached 18.70, 206.10, 243.50 and 360.70 gm for 0, 100, 200 and 300 micrograms the treatments respectively. In the current investigation there was significant reduction in levels of blood glucose, insulin hormone for the 2nd,3rd ,4th groups of rats when compared to the control group (table 3).The blood sugar were 120.10, 116.9,99.0, 89.3 mg/dl and Insulin hormone rates which were 0.569,0.498, 0.481,0.389µg/L respectively. Also, the results of the current study showed that there was a significant decrease in levels of SOD for the 2nd ,3rd , 4th groups of rats which were 1.867,1.583, 1.042U/ml in compared to the control group 2.151U/ml. While there was a significant elevation in levels of MAD for the 2nd, 3rd, 4th groups of rats which were 0.764,0.911,1.516U/ml in comparison of the control group 0.616 U/ml (table 3) . As for sexual hormones, the results released from table (4) there was a significant elevation in levels of FSH, LH, Testosterone and inhibin hormones to the 2nd,3rd,4th group of rats in compared to the control group. FSH concentrations were 2.25,4.45, 5.30, 6.15 U/ml respectively. Also, the levels of LH which were 31.35,45.04,51.065,57.11ng/ml respectively. The concentration of testosterone hormones was 0.555,1.580, 1.865, 2.585ng/ml. As far as there was a significant increase in levels of Inhibin hormone in the 2nd,3rd,4th group of rats which were 4.440,5.345, 6.845 pg/ml in comparison to the control group 3.685pg/ml (table 4).

Discussion

In the current investigation, the levels of hemoglobin, glucose, RBC, and WBC were significantly higher in groups of rats treated with varying amounts of sorbitol than in the control group. These findings are consistent with results of Abukhomra et al. [19], who observed a marked rise in RBC, hemoglobin, WBC, glucose levels in rats were treated with varying concentrations of sorbitol relative to the control group. This increase may be explained by sorbitol's potential to cause damage via oxidation. Hematological indicators offer a sufficient foundation for evaluating the illness, the antioxidant defense mechanisms' reaction, degree of tissue damage and the experimental animals' health [24]. There was a notable decrease in the levels of PCV in the current investigation. This observation conflicts with that of Abukhomra et al. [19] who reported a notable elevation in PCV levels in sorbitol-treated rats relative to the control group which may be due to sorbitol's oxidative damage to RBCs and hemoglobin. The results of the statistical analysis in the current study indicated a significant decrease in neutrophil levels and a significant increase in concentrations of lymphocytes and mononuclear cells in groups of rats treated with different levels of sorbitol compared to the control group. These results are consistent with those of Rosalovsky [25] who reported a significant increase in lymphocyte and monocyte levels in the sorbitol-treated rats compared to the control group.

Hematological parameters	First group (Control) Mean ± S.E. (0 µgm)	Second group Mean ± S.E. (100 µgm)	Third group Mean ± S.E. (200 µgm)	Fourth group Mean ± S.E. (300 µgm)
No. of samples	10	10	10	10
RBC($\times 10^6$) corpuscles	6.47 ± 0.06 c	7.22 ± 0.03 b	7.16 ± 0.12 b	7.78 ± 0.02 a
Hb (gm/dl)	13.32 ± 0.05 d	13.50 ± 0.02 c	13.82± 0.01 b	14.62 ± 0.03 a
PCV (%)	41.47 ± 0.14 a	38.29 ± 0.08 b	34.49 ±0.26 c	33.53 ± 0.23 d
WBC($\times 10^3$) cells.	8.35 ± 0.04 d	9.47 ± 0.02 c	9.86 ± 0.03 b	10.68 ± 0.11 a
Lymphocytes(%)	65.56 ± 0.15 d	66.37 ± 0.25 c	69.81± 0.27 b	71.43 ± 0.32 a
Neutrophils (%)	22.51± 0.16 a	21.19 ± 0.15 c	21.81 ± 0.21 b	20.50 ± 0.21d
Monocytes (%)	6.27 ± 0.06 c	6.47 ± 0.03 b	6.90 ± 0.01 a	6.97 ± 0.02 a
ESR (mm/hour)	2.39 ± 0.06 a	2.11 ± 0.06 b	1.97 ± 0.02 c	1.85 ± 0.01 c
Clotting time (sec)	36.02 ± 0.37 d	46.76 ± 0.52 c	57.14 ± 0.45 b	77.96 ± 0.29 a
Bleeding time(sec)	58.56 ± 0.74 d	72.04 ± 1.04 c	85.86 ± 0.45 b	112.11 ± 0.53a

The different letters in the raw means presence of significant differences at (P≤0.05) .
S.E. : Standard Error . RBC: Red Blood Cells . WBC: White Blood Cells.
Hb: Hemoglobin level , PCV: Packed Cell Volume.
Table 1: Effect of dossing with different levels of sorbitol on hematological parameters of Wistar rats.

Body weight (gm)	First group (Control) Mean ± S.E. (0 µgm)	Second group Mean ± S.E. (100 µgm)	Third group Mean ± S.E. (200 µgm)	Fourth group Mean ± S.E. (300 µgm)
No. of samples	10	10	10	10
Initial weight (gm)	253.80 ± 1.03 a	254.90 ± 1.00 a	253.50 ± 1.43 a	255.20 ± 1.44 a
Final weight (gm)	185.70 ± 2.10 d	206.10 ± 0.67 c	243.50 ± 0.56 b	360.70 ± 0.72 a

The different letters in the raw means presence of significant differences at (P≤0.05) .
S.E. : Standard Error.
Table 2: Effect of dossing with different levels of sorbitol on body weights of Wistar rats.

Biochemical parameters	First group (Control) Mean ± S.E. (0 µgm).	Second group Mean ± S.E. (100 µgm)	Third group Mean ± S.E. (200 µgm)	Fourth group Mean ± S.E. (300 µgm)
No. of samples	10	10	10	10
Blood glucose (mg/dl)	120.1 ± 0.77 a	116.9 ± 0.57 b	99.0 ± 1.49 c	89.3 ± 0.52 d
Insulin (µg/L)	0.569 ± 0.0071 a	0.498± 0.0068 b	0.481± 0.0053 b	0.389± 0.0081 c
SOD (U/ml)	2.151± 0.01 a	1.867± 0.013 b	1.583± 0.014 c	1.04± 0.014 d
MDA (U/ml)	0.616± 0.013 d	0.764 ± 0.005 c	0.911 ± 0.013 b	1.516 ± 0.01 a

The different letters in the raw means presence of significant differences at (P≤ 0.05) .
S.E. : Standard Error . SOD : Superoxide Dismutase MDA: Malondialdehyde .
Table 3: Effect of dossing with different levels of sorbitol on biochemical parameters of Wistar Rats.

Sexual Hormones	First group (Control) Mean ± S.E. (0 µgm)	Second group Mean ± S.E. (100 µgm)	Third group Mean ± S.E. (200 µgm)	Fourth group Mean ± S.E. (300 µgm)
No. of samples	10	10	10	10
FSH (U/ml)	2.25 ± 0.15 d	4.45 ± 0.05 c	5.30 ± 0.10 b	6.15 ± 0.05 a
LH (ng/ml)	31.35 ± 0.10 d	45.04 ± 0.18 c	51.065 ± 0.59 b	57.11 ± 0.13 a
Testosterone (ng/ml)	0.555 ± 0.01 d	1.580 ± 0.04 c	1.865 ± 0.025 b	2.585 ± 0.04 a
Inhibin (pg/ml)	3.685 ± 0.05 d	4.440 ± 0.08 c	5.345 ±0.12 b	6.845 ± 0.01 a

The different letters in the raw means presence of significant differences at (P≤ 0.05) .
S.E. : Standard Error . FSH : Follicle Stimulating Hormone . LH: Luteinizing Hormone .
Table 4: Effect of dossing with different levels of sorbitol on sexual hormones of Wistar rats

The reduction in levels of neutrophils may be attributed to oxidative damage of sorbitol on these types of WBC which are present in the whole body either in the lymphatic system or in the blood stream. These cells strengthen the animal's immune system, and which are produced in the bone marrow. The WBCs protects animal bodies from external and internal invaders such as different types of bacterial spp., viruses, protozoa, parasites and certain types of tumor cells and other different diseases [26].

The animals in the 2nd, 3rd, and 4th groups in the current study experienced a significant decrease in final weight compared to the control group after receiving varying levels of sorbitol treatment. This reduction in weight may be attributed to osmotic diarrhea which is a side effect of sorbitol treatment and causes frequent intestinal perfusion which dehydrates of the animal body [3].

Comparing the 2nd, 3rd, and 4th groups of rats treated with varying dosages of sorbitol to the control group there was a notable decrease in blood glucose levels. This result is consistent with that of Chukwuma and Islam [27] who found that rats treated with sorbitol had significantly lower serum glucose levels. These results

may be explained by effects of sorbitol on blood glucose levels which in both normal and type 2 diabetic rats increase muscle glucose uptake ex vivo and inhibit intestinal glucose absorption ex vivo. In contrast Abukhomra et al. [19] reported that the glucose levels will be elevated in the sorbitol treated rats. Because sorbitol causes oxidative damage to the B-cells of the pancreas which are responsible for producing insulin [19,28] the present study's results indicate a considerable fall in insulin levels in the sorbitol-treated rats.

The sorbitol had a significant effects on the hematological parameters and on the levels of glucose in the serum of the animals , as well as on the levels of some of the sexual hormones. It is recommended not to consume excessive sorbitol in the diet.

Compliance with Ethical Standards:

Approval of this study was obtained from the Ethics Committee of the College of Veterinary Medicine at the University of Mosul. The procedures used in this study adhered to the principles of the Declaration of Helsinki.

Acknowledgements

Authors show gratitude to the deanships of the College of Veterinary Medicine / Al-Qasim Green University and the College of Agriculture and Forestry / University of Mosul for their support and encouragement and providing us with scientific research that helped us to complete scientific research.

Author contributions

This study included the contribution of Dr. Zahraa H.K. Al-Moussawi in preparing the concept of the study, collecting data, providing experimental materials and design of the experiment, while participation of Dr. Mozhir K.K. Almahdawi in statistical analysis of the data, collecting blood samples, and laboratory analysis. Writing the article and first draft of the manuscript. The contribution of Dr. Abdul Sattar S.S. Al-Bayati included data collection, statistical analysis of data, interpretation of statistics, and writing of literature related to the subject of this study. All authors had a contribution in commenting on the study's literature and revising it and in conclusion, the authors agreed to prepare the manuscript for publication.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

References

1. Basmaa SS, Nevzat A, Mahmoud AA, Omar FA. Some Alternative Sweeteners (Xylitol, Sorbitol, Sucralose and Stevia):Review. Karaelmas Science and Engineering Journal, (2014);4(1):63-70.
2. Rajam MG Seeni. Impact of Organic Cultivation in Tamil Nadu. Agriculture and Food: E-newsletter, (2021);3(6);166-169.
3. Islam Md. Shahidul, Ei S. Sorbitol-based osmotic diarrhea: Possible causes and mechanism of prevention investigated in rats. World Journal of Gastroenterology, (2006); December 21; 12(47): 7635-7641.
4. Awuchi Ch. Godswill. Sugar Alcohols: Chemistry, Production, Health Concerns and Nutritional Importance of Mannitol, Sorbitol, Xylitol and Erythritol. International Journal of Advanced Academic Research, (2017); 3(2): 2488–2849.
5. Zhang Yi, Tong Ch , Gang Z, Gongying W, Hua Z. Efficient production of isosorbide from sorbitol dehydration over mesoporous carbon-based acid catalyst. Applied Catalysis A: General, (2019); 575(1), 38-47.
6. Nicoud L, Cohrs N, Arosio P,Norrant E, Morbidelli M. Effect of polyol sugars on the stabilization of monoclonal antibodies. Biophysical Chemistry, (2015); 197(1): 40–46.
7. Mooradian AD, Meridith S, Masaaki T. The role of artificial and natural sweeteners in reducing the consumption of table sugar: A narrative review. Clinical Nutrition ESPEN, (2017); 18:1-8.
8. Eugenio A, Mathilde C, Isabella E, Maria LC, Emanuela B, Franco B, Flavia G. Sweet taste in apple: the role of sorbitol, individual sugars, organic acids and volatile compounds. Scientific Reports, (2017); 7:44950.
9. Bakshi RA, Shaziakhanday ZS, Khan DBN. Physiochemical and rheological characteristics of sorbitol low sugar cherry jam. Journal of Postharvest Technology, (2022); 8(3): 61-70.
10. Adkison K, Wolstenholme A, Lou Y, Zhang ZE, Perger T, et al. Effect of Sorbitol on the Pharmacokinetic Profile of Lamivudine Oral Solution in Adults: An Open Label, Randomized Study. Clinical Pharmacology and Therapeutics, (2018); 103(3): 402-408.
11. Yang S, Yaya Z, Junjing Y, Zhiqin F, Si TG, Hong T , Lei P. Sugar Alcohols of Polyol Pathway Serve as Alarmins to Mediate Local-Systemic Innate Immune Communication in Drosophila. Cell Host Microbe, (2019); 14(2): 240-251.
12. Kloub SM, Banihani S., Atrooz O, Hananeh W. The Effect of Alcoholic Extract of Anabasis syriaca Iljin on Biochemical and Histological Parameters in Rats. Journal of Toxicology,(2022); Article ID 6945745.
13. Chen JL, Tian LL, Li ZY, Wang LX, Guo Y, et al. Molecular characterization and phylogenetic analysis of a novel Porcine epidemic diarrhea virus circulating in large-scale pig farms in Xinjiang, China. Kafkas Üniversitesi Veteriner Fakültesi Dergisi, (2023); 29 (4): 373-380.
14. Shin HJ, Heijin L, Hyo-Seok Na.The effect of a mixture of 2.7% sorbitol-0.54% mannitol solution on blood coagulation: an invitro, observational healthyvolunteer study using rotational thromboelastometry (ROTEM). Korean Journal of Anesthesiology, (2019); 72(2), 143–149.
15. Kondo N, Fuko H, Takashi T. Evaluation of 3-Borono-L-Phenylalanine as a Water-Soluble Boron Neutron Capture Therapy Agent. Pharmaceutics, (2022);14(5): 1106-1118.
16. Darko E,Végh B, Khalil R, Marček T, Szalai G, Pál M, Janda T.Metabolic responses of wheat seedlings to osmotic stress induced by various osmolytes under iso - osmotic conditions. PLOS ONE, (2019); 4(12): 226151.
17. Al-Kadhi N, Ali EKh, Ibrahim RNKh, Kasim SA, Qays SA. Antioxidant effect of Gundelia Tournefortii Extract on Some Physiological, Biochemical and Histopathological Changes in Male Rats. The Journal of Research on the Lepidoptera, (2020); 51(1): 479-495.
18. Hu B, Guo X, Li Y, Cheng A, Liu J, Lu Q.Reaction characteristics and mechanisms of sorbitol fast pyrolysis. Journal of Fuel Chemistry and Technology, (2021); 49(12): 1821–1831.

19. Abukhomra AS,Al-Awady HG,Al-Charak AH.Effect of different doses of sorbitol on hematological parameters and blood glucose of rats.Journal of Pharmaceutical Negative Results, (2022); 13(1): 1765-1771.
20. Weiser G, Mary AT, Glade W, Robin W, Allison TW.Sample Collection, Processing, and Analysis of Laboratory Service Options In: Thrall M.A., Veterinary Hematology and Clinical Chemistry. 2nd ed. Ames, Wiley-Blackwell, (2012): 34-38.
21. Al-Zubaidy KM, Al-Falahy MA.Principles and procedures of statistics designs and experimental designs. Ministry of Higher Education And Scientific Research, University of Duhok, College of Agriculture,(2016); page:(183-187). Kurdistan Region , Iraq .
22. Statistical Analysis System Inc SAS. User's Guide Introduction to Analysis of Variance Procedures, Statistics, Cary NC,(2012); Release 12.1,Tsozo North Carolina State University of Cary, NC USA.
23. Duncan DB. Multiple range and multiple F tests. Biometrics,(1955); 11: 1- 42, USA .
24. Joseph L, Evans ID, Goldfine BA, Maddux GMG, Grodsky. Oxidative Stress and Stress-Activated Signaling Pathways: A Unifying Hypothesis of Type 2 Diabetes. Endocrine Review, (2002); 23(5): 599-622.
25. Rosalovsky VP. Hematological indices of rats during the first hour after chlorpyrifos exposure. Hematological indices of rats during the first hour after chlorpyrifos exposure. Biological Bulletin, (2015); (1): 123- 132.
26. Yang S, Yaya Z, Junjing Yu, Zhiqin F, Si-tang G, Tang H, Pan L. Sugar Alcohols of Polyol Pathway Serve as Alarmins to Mediate Local-Systemic Innate Immune Communication in Drosophila. Cell Host & Microbe, (2019); (26): 240–251.
27. Ifeanyi CC, Islam MS. Sorbitol increases muscle glucose uptake ex vivo and inhibits intestinal glucose absorption ex vivo and in normal and type 2 diabetic rats. Applied Physiology Nutrition and Metabolism, (2017); 42(4): 377-383.
28. Mehdi HA, Ban TM, Abbas MB. Effect of Nano-Silvers,Nano Zinc Oxide and Benomyl Pesticide on some Physiological Properties of Sclerontina Sclerotiorum. Biochemical Cellular Archives, (2017); 18(2): 2181-2196.