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ROLE OF FRESH CARROT JUICE AGAINST CISPLATIN TOXICITY ON SPLEEN AND SOME BLOOD PARAMETERS IN RABBITS

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ABSTRACT

The current research targeted to study the role of the juice of the carrot against cisplatin toxicity in the spleen of male rabbits by using a single injection of cisplatin in an intraperitoneal of 5 mg/kg. The parameter counts of WBCs, PLT, LYM, MID, and GRA and the level of C3 complement protein were measured. The result showed changes in the hematological parameters in the group of CP treated and the group of CP treated with oral fresh carrot juice paralleled to the control group. WBCs and PLT count in serum samples show an important P- value < 0.05 decrease in the serum of rabbits treated with cisplatin paralleled to the negative control group. Moreover, there were decreases in LYM and MID counts but non-significant in the serum rabbits treated with CP paralleled to the group of negative control. However, the GRA count and level of C3 complement were increased in the serum rabbits treated with CP paralleled to the control negative group. After rabbits received an oral dose of fresh carrot juice 5ml/kg for the following 4 days before cisplatin injection, 3 following days after cisplatin injection, the level of C3 complement and counts of GRA were reduced in the group of CP-treated with oral fresh carrot juice, and succeeded in restoring the level of C3, count of GRA to the same range to the negative control. Moreover, the count of LYM slightly increased compared to the group of CP treated but not in the same range as the negative control. However, other parameters show no effect of the fresh carrot juice treatment.

Furthermore, for histopathological investigation, the spleen from all groups was collected. Histological observations of spleen show that fresh carrot juice has the role reduced the toxicity of cisplatin by reduce the effect of cisplatin in

the tissues which reduce number of the white cells in red and with pulp. This study demonstrated that fresh carrot juice has a role as a potential therapeutic against (CP) toxicity in the immunity of rabbits.

1.0 Introduction

Cisplatin (CP), or the cisplatinum also known as Cis-Diamminedichloroplatinum 2, is a highly effective cancer drug, permitted in 1978 by the Food Drug Administration (Kelland 2007). It is a well-known chemotherapy that is widely given to treat many solid organ tumors, such as those in the head and neck, lung, and bladder cancers, as well as leukemia, breast, testicular, ovarian, kidney, and brain cancers. It is effective against several types of cancer, for example, lymphomas, germ cell tumors, carcinomas, and sarcomas.

Chemotherapeutic drugs are the most commonly used treatments for malignant tumors due to their cytotoxic effects, that lead to tumor cell death via directly damaging DNA or inhibiting cell division, thus, these drugs are typically nonspecific, leading to widespread tissue toxicity (Blanchard 2012). Cisplatin is considered as a cytotoxic drug that affects cells by disrupts with DNA repair, causing DNA damage, inhibiting DNA synthesis and mitosis, and inducing apoptotic cell death (Wang and Lippard 2005). Inflammation and oxidative stress play an essential roles in cisplatin-induced pathophysiology (Rahman *et al*, 2006). Cisplatin prompts numerous side effects, for instance ototoxicity, myelosuppression, gastrotoxicity, and allergic reactions (Casanova *et al*, 2020), in addition, neurotoxicity and hemolytic uremic syndrome (Scott *et al*., 1995; Vandendries and Drews, 2006).

Carrots are one of the plant sources of vitamin A, which enhances immune function, contributes to immune system development, and plays an important role in both cellular and humoral immune responses. In addition, vitamin A is vital for adaptive immunity, aiding in the growth of T-type helper (Th) B cells, and its lack can lead to a reduced response mediated by antibodies directed via Th2 cells (Stephensen 2001).

Carrots generally contain several biologically active compounds, including beta-carotene, phenolics, carotenoids, polyacetylenes, and vitamin C. These compounds obligate several immunomodulatory properties due to their regulatory properties of both innate and adaptive immune responses, as well as their anti-oxidative and anti-inflammatory. The immunomodulatory activities include inhibition and promotion of inflammatory cytokines, antioxidants, and enhancement of endogenous antioxidant defense, in addition to reducing pathways signaling proinflammatory and anti-inflammatory. Moreover, the immune effects of carrots include regulation of leukocytes, antibodies, and histamine (Anjani *et al*., 2022). Moreover, a study conducted by Al-Sanafi, 2017, showed that carrots have an effective role as antioxidants, antidiabetic drug, antimicrobial, and antihepatotoxic, antinephrotic, anticardioprotective, and anti-inflammatory, in addition to their wound-healing properties. In a review by Chen *et al*., 2021, the effect of beta-carotene protection against gastric cancer has been reported based on epidemiological surveys. Carrots can enhance immunity and the health of the eye, as noted by Silva-Dias (2014) and Shakil *et al*., (2017).

Although the particular immune activities are not well studied, despite various studies that have discussed the benefits of the bioactive compounds found in carrots (Silva-Dias 2014), the mechanism is known to be very complex and still unclear. The biochemical components of carrots have not yet been studied in detail by many researchers for their bioactive properties, including antioxidant, activities of anti-inflammatory, and immunomodulatory.

The toxicity of cisplatin in the spleen and its harmful effect on the spleen had not yet been determined, considering that the spleen is the largest and most important lymphoid organ in the immune system.

The histoquantitative effect of the spleen of rats exposed to cisplatin compared to normal spleen was studied by Milićević *et al*, 1994, and showed the red and the white pulp zones and the marginal zone were significantly decreased in the organ that was exhibited to cisplatin. In addition, in the section area of the spleen, the numbers and the density of the follicles were significantly decreased. A study by Wang *et al*, 2010 shows that low-dose cisplatin leads to erythrocyte damage and accumulates in the red pulp of the spleen with imperfect recycling of FPN1 and defective ferritin, leads to iron excess in the spleen cells, and causes hemosiderin deposition in splenic tissue.

The complement system plays an effective role in innate immunity, and consists of a large number of different plasma proteins cofactors, and receptors. Activation of complement pathways induces convertases that cleave the C3 and C5 proteins, effects on immunity, and inflammation-promoting tumors (Reis *et al.,* 2019; Reis *et al*., 2018). It has been informed that linking treatment of cytotoxic with the complement signaling barrier in patients with negative triple of breast cancer, which is a kind of breast cancer, may weaken the opposing chemotherapy effects (Monteran *et al*., 2022).

It was supposed that the complement assisted the body to recognize and eliminate the change in the cells, but it has been shown complement activation contributes to tumorigenesis and can also help tumors evade immune elimination (Thurman *et al*., 2020). In different types of cancer, the activation of complement occurs by 3 major pathways: classic, alternative and lectin pathways, and fragments of complement have many effects on cancer and during the tumor micro-environment (Thurman *et al*., 2020). Aim of this current research was to study the role of fresh carrot juice against cisplatin toxicity on spleen and some blood parameters in male rabbits. The level of complement C3 and some hematological indicators were measured in rabbit serum with cisplatin 5mg/kg.

2.0 Materials and methods:

2.1 Chemicals:

Cisplatin injection with dose 50 mg/50 ml was used to inject rabbits and create a model affected by cisplatin toxicity.

2.2 Plant Material

Fresh carrot roots were used in this study. They were chopped after being cleaned and put into the apparatus to prepare juice with no added water. The daily juice of carrot was prepared until the end of the experiments.

2.3 Experimental Animals:

15 male rabbits whose weights ranged between 1000 – 1900 g each were used in the study. All rabbits were divided into groups and were housed in cages in the laboratories of Sirte University. The animals were observed for several days before the experiment started in order to ensure their health and to adapt to the new laboratory environment. All rabbits were subjected at all stages of the experiment to the same laboratory conditions of ventilation, lighting, and temperature. They were in good health, and they were given water and food continuously and in appropriate quantities during the duration of the experiment with a commitment to regular hygiene.

2.4 Design of the experiment:

The experiment was designed by randomly dividing every 15 experimental rabbits into three groups. Group 1 rabbit (G1) was defined a negative in which given a dose of 0.9% saline solution intraperitoneally (control). Then this group of rabbits was injected orally with a dose of 5 ml of distilled water for 4 days, and on the fourth day, 5 ml/kg of saline solution was injected into the abdominal cavity. Then the distilled water injection was continued for 3 successive days after the saline solution injection to stabilize the experiment. The second group (G2) was a positive control or group of Cisplatin-treated. In this group the rabbits were dosage orally with a dose of 5 ml of distilled water for 4 days; on day 4, rabbits injected intraperitoneally with a cisplatin solution of 5mg/kg body-weight, as mentioned in the study by Okoko and Oruambo (2008) and another study by Yasuyuki et al,1991. After that, the distilled water injection was continued for 3 successive days, after the cisplatin injection. The third rabbit group (G3) was dosage with the juice of a fresh carrot at a dose of 5 mL/kg body-weight by gavage orally for successive 4 days, earlier the injection with cisplatin and successive 3 days later the injection with the cisplatin.

The experiment ended after a 7-day injection period. The rabbits were slaughtered after fasting for 12 hours, they had access just to water, then the blood and the spleen were collected. The blood samples were collected in centrifuge tubes of the type containing EDTA to prevent blood clotting and to conduct blood measurements of CBC, which include white blood cells (WBCs/µl), platelets (PLT/µl), and lymphocyte count (LYM); also (GRA) include neutrophils, monocytes, eosinophils, and basophils. Moreover, mid-range absolute counts (MID) cells were identified using an electronic blood analysis device (R800 system). Moreover, the blood samples were collected without anticoagulants for serum separation for the C3 complement test.

2.5 Histological examination:

Spleen samples from all treated groups of rabbits were carefully removed and washed with normal physiological saline, then the samples were dried with filter paper and, after that,

rapidly fixed in a solution of 10% formalin. The samples were dehydrated with alcohol at ascending concentrations and then embedded in paraffin wax. All the spleen sections were cut into several thin sections to 5 µm in thickness. After that, all the sections were add hematoxylin and eosin staining, which can be examined all the sections under a bright microscope via a pathologist who is uninformed of the conditions of all the samples.

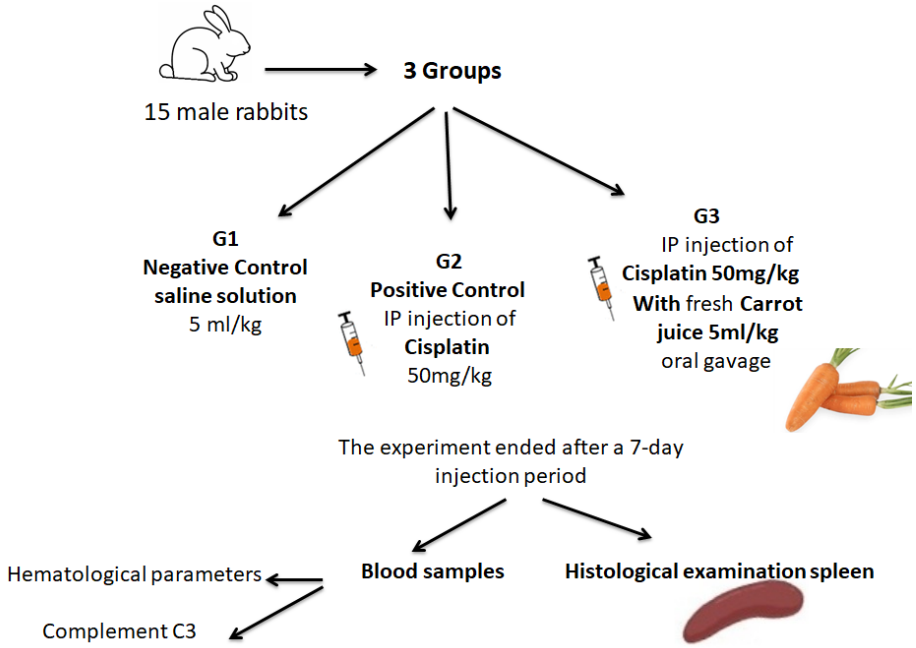

Figure (1) Schematic overview of the method.

2.6 Statistical analysis:

The data in this current study were examined by the program SPSS. All values data were noted as Mean with Standard Error, while, the test One-way ANOVA was used to parallel the mean of the groups. Values of *P value* < *0.05* were deemed significant (Steel and Torrie1980).

3.0 Results Discussion

3.1 The hematological parameters

The complete blood count was conducted for the following hematological parameter values: White blood cells (WBCs), lymphocyte (LYM), platelets (PLT), Mid-range absolute count (MID), and Granulocyte (GRA). As shown in Table 1 and Figures 2,3,4,5& 6, the CP management dose I.P of 5 mg/kg. caused in changes in the hematological parameters in the group of CP treated and the group of CP treated with oral fresh carrot juice compared to the negative control .

WBCs count showed a significantly decreased (P value < 0.05) in the group treated with CP (as positive control) and in the group treated with carrot juice 5.6±0.27, 5.2±1.08 respectively paralleled to the negative control group 8.2±0.98 (Table 1 and Figure 2). However, there was

no important difference in the WBCs count of the group treated with carrot juice 5.2±1.08 when compared to the positive control group 5.6±0.27.

Table (1) Effects of carrot juice on WBCs, LYM, PLT, MID, GRA and serum C3 protein in control group and group treated rabbits. (all the values are expressed as Means ± SE).

Parameters	(G1) Control	(G2) Cisplatin	(G3) Cisplatin & Carrot
WBC	8.2±0.98	5.6±0.27*	5.2±1.08*
LYM	4.08±0.44	2.45±0.20	2.91±0.79
PLT	314.2±53.3	186.8±23.2*	164±30.71*
MID	1.13±0.0578	0.48±0.0338	0.41±.01193
GRA	2.2550±0.114	2.6200±0.086	1.9260±0.185
C3	0.17±0.025	0.21±0.029	0.18±0.004

All the values above are expressed for 5 rabbits in each group as mean ± SE.
* Significance (P value <0.05) when paralleled to the negative control group (group 1 control (G1)

Lymphocyte count was lower in rabbits treated with CP paralleled to the control group. However, when rabbits that treated with CP received the oral juice of carrot, the lymphocyte count was less compared to a group of CP treated. there is no important difference (P value > 0.05) in lymphocyte count between all groups (Table I and Figure 3). The fresh carrot juice caused an increased lymphocyte count compared to a group of CP treated without fresh carrot juice.

Platelet count in Table 1 and Figure 4 shows a significant (P value < 0.05) reduction in the CP group (186.8 ± 23.2) and in the group treated with carrot juice (164 ± 30.71) paralleled to the group of negative control.

As shown in Table 1 and Figure 5, the granulocytes (GRA) count appeared higher in CP-treated rabbits paralleled to the group of negative control, reduction (P value > 0.05) in GRA value of CP- treated rabbits when received juice of carrot orally with 5ml/kg body-weight paralleled with the group of positive control. However, no important elevation (P value < 0.05) in GRA value was observed in CP-treated rabbits. When rabbits given the juice of carrot cure orally with cisplatin, the value of GRA was less compared to the group of CP treated and similar to the group of negative control. The parameter Mid-range absolute count (MID) count was reduced in both the CP-group and in the group-treated with carrot juice paralleled to the group of negative control (table 1 and Figure 6) there is no important difference in MID count between all groups. However, there was no important difference shown in rabbits blood of the group treated with CP paralleled to the group of cisplatin treated with juice of fresh carrot.

The same observation was shown in the Table 1 and Figure 7, the level of C3 complement appeared higher in the group treated with CP paralleled to the group of negative control but there was no significant with P value >0.05 elevation in serum C3 complement level observed in CP-treated rabbits. On the contrary, when rabbits received the orally juice of carrot, the level of C3 complement was less paralleled in the CP-treated group and stayed

similar to the level of the negative control. The juice of fresh carrot caused a decrease in the in the level of C3 complement in the serum, same as in the group of negative control.

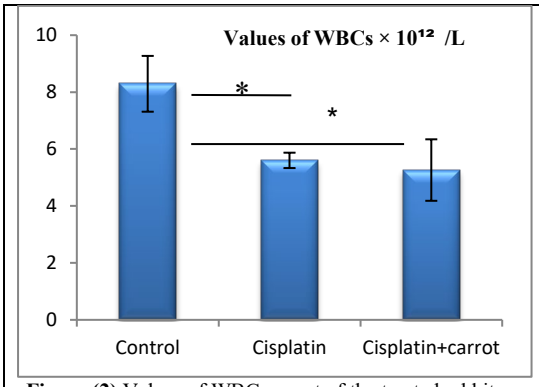

Figure (2) Values of WBCs count of the treated rabbits group paralleled to the control.

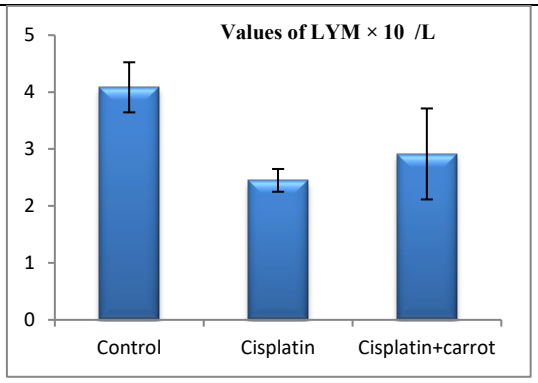

Figure (3) Values of LYM count of the treated rabbits group paralleled to the control.

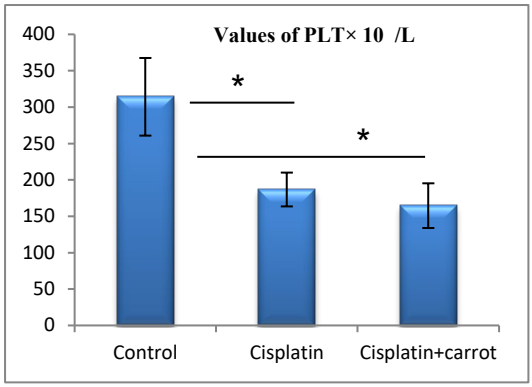

Figure (4) Values of PLT count of the treated rabbits group paralleled to the control group.

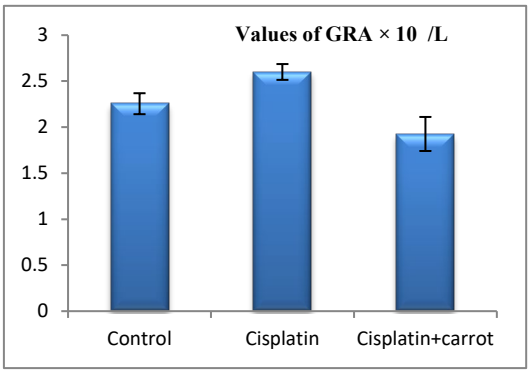

Figure (5) Values of GRA count of the treated rabbits group paralleled to the control group.

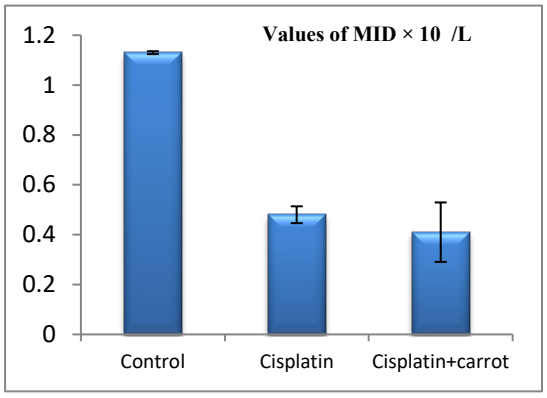

Figure (6) Values of MID count of the treated rabbits group paralleled to the control.

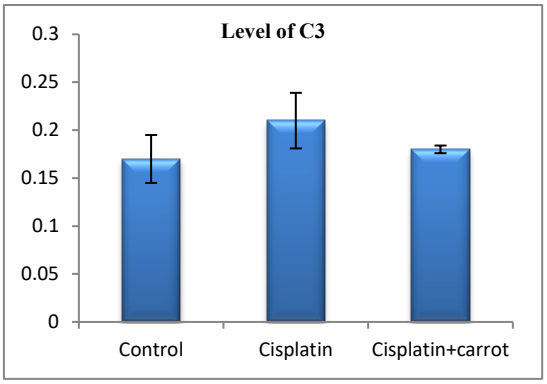

Figure (7) Values of C3 level of the treated rabbits group paralleled to the control.

3.2 Histological observations

To investigate whether carrot juice has any effect on the spleen tissue and also to emphasize the negative impact of cisplatin on the spleen tissue architecture. The tissues were stained with hematoxylin and eosin stain and observed under a bright microscope.

Examination of the spleen sections (Figure 8) as can be seen in negative control rabbits showed normal histological architecture. The connective tissue capsule of the spleen and both RP and WP parenchymal components are clearly visible. The splenic trabeculae form a pathway for branches of the splenic artery, which central arteries divide to enter the pulp. Both white pulp and red pulp were structurally clearly identified, with normal cell density. The central artery and germinal center were clearly visible in the WP, and the marginal zone separated the WP from the RP. The WP is consist of subcompartments of the periarteriolar lymphoid sheaths (PALS) and the follicles, which both appeared normal in negative control (Figure 8).

In the spleen of negative control rabbits, the red pulp consists mostly of the splenic sinusoids and aggregation of some different cell types. The white pulp represents dense aggregates of lymphocytes .

In the negative control, there were some Hemosiderin deposits in the RP, and occasionally in the WP too (Figure 8 panel B arrow). Both pigments hemosiderin and ferritin are the most popular in the macrophages of the RP (Losco 1992).

On the other hand, the spleen sections from the rabbits group treated with cisplatin and the group with fresh carrot juice with CP-treated rabbits revealed obvious pathological changes, histopathological changes in the spleen were characterized by disorder of lymphatic follicles; in the WP there is hyperplasia with certain necrotic cells in both the WP and RP. Moreover, hemosiderosis was higher along with fibrosis in the RP; in addition, certain lymphatic follicles were also observed.

As shown in Figure 9 panel B and D it was observed that there are further Granulocytes (neutrophils) in the RP in the sections of spleen from the rabbits group treated with cisplatin (positive control group) compared to the group with fresh carrot juice with CP-treated rabbits (Figure 10 panel B) and negative control groups. This same observation was noted in Figure 5 the values of GRA count, the granulocyte count appeared higher in cisplatin treated rabbits paralleled to the group of negative control and the group with juice of fresh carrot with cisplatin treated rabbits.

Spleen sections for rabbits of study groups treated with cisplatin show the PALS areas also marginal zones have expanded and augmented cellularity and there is a comparative reduction in the zone of RP because of the increase of the WP along with increased hemosiderin deposits in the red pulp consistent with increased red cell damage, moreover, in the red pulp dense outgrowth of new splenic sinuses (Figure 9) when paralleled to group of negative control (Figure 8) and group of fresh-carrot juice with CP-treated rabbits (Figure 10).

Histological characteristic changes of the spleen were seen after the cisplatin was given to rabbits. The control of rabbit tissue showed a separate region of WP enclosed by RP and marginal zone, whereas the tissue of rabbits given cisplatin treatment exhibited deposition of hemosiderin; this is a damaged typical of the spleen, and in addition, the boundary between

WP and RP was unorganized, which shows the effect toxicity of the drug on architecture tissue.

In normal spleen show exhibits aggregates of lymphocytes in the white pulp surrounded by a well-vascularized, less densely cellular red pulp however, this exhibits aggregates were more densely irregular, and scattered in spleen from the rabbits group preserved with cisplatin paralleled to the group with fresh carrot juice with CP-treated rabbits and negative control groups. It has been observed that trabecula from connective tissue runs throughout the spleen more in in spleen from the rabbit group treated with cisplatin compared to in spleen from the rabbit group treated with cisplatin, this trabecula provides an expressway for blood vessels to go into and leave the splenic tissue.

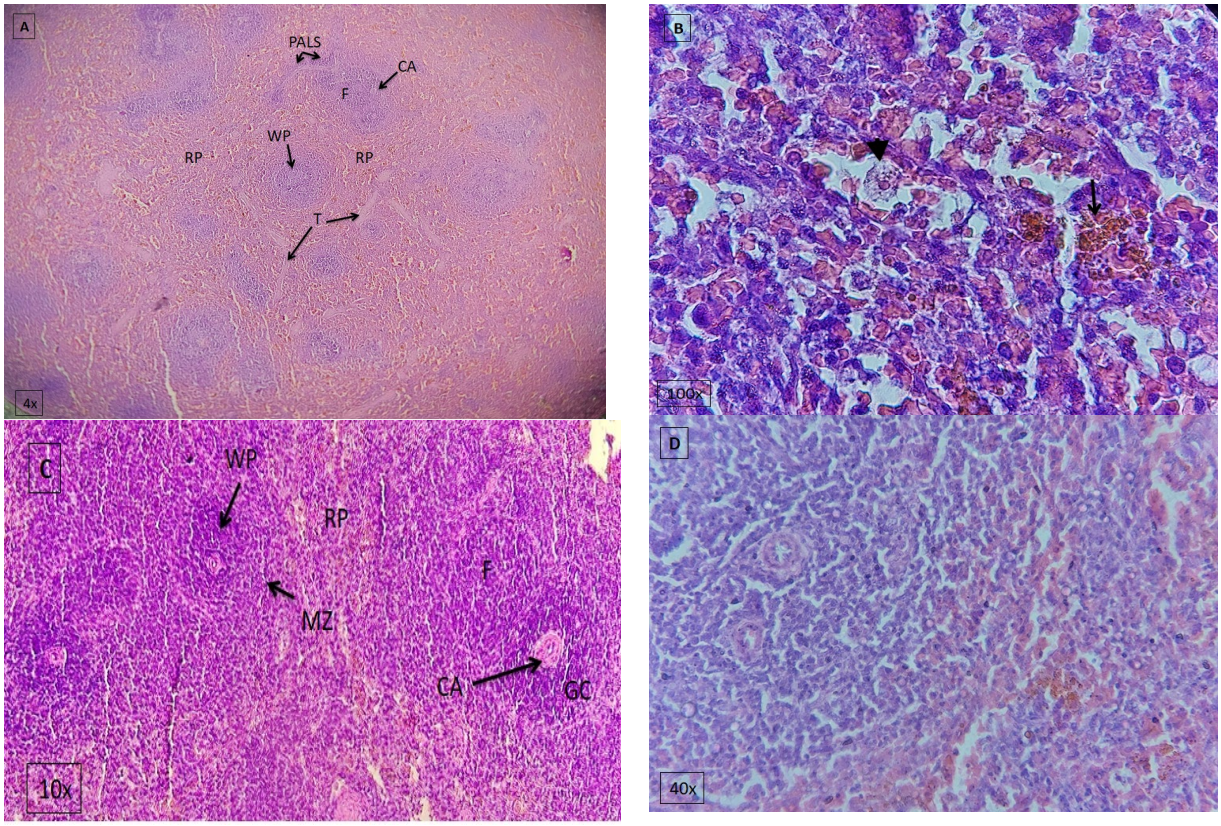

Figure (8) The histological spleen examination of the group negative control rabbit. In the normal splenic histology, the spleen is the contained zone of the pulps red and white and marginal zone. Representative images of the spleen sections demonstrated the different magnification. Panel (A) magnification of 4X shows normal histological architecture. Panel (B) show hemosiderin (arrow) and white cells (head arrow). Panel (C) 10X and 40X in Panel (D). White Pulp(WP); Red Pulp(RP), (CA =Central Artery, (T) = Trabeculus, (MZ)=marginal zone, F =Follicle, GC = germinal center. Periarteriolar Lymphoid Sheath (PALS). Haematoxylin and eosin staining were used.

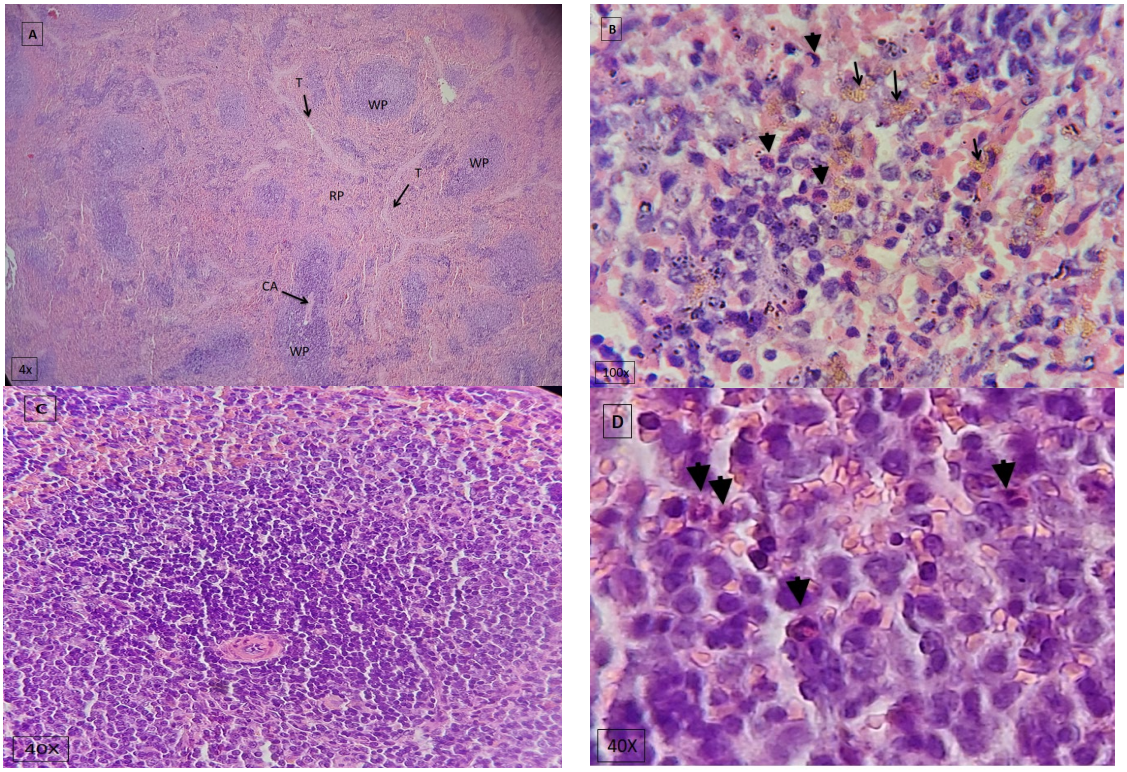

Figure (9) The histological spleen examination of the rabbit group treated with Cisplatin. Representative images of the spleen sections demonstrated the different magnification. Panel (B) 100X show hemosiderin (arrow) and white cells (GRA) (head arrow). Panel (D) and (B) white blood cells neutrophils (arrow head).

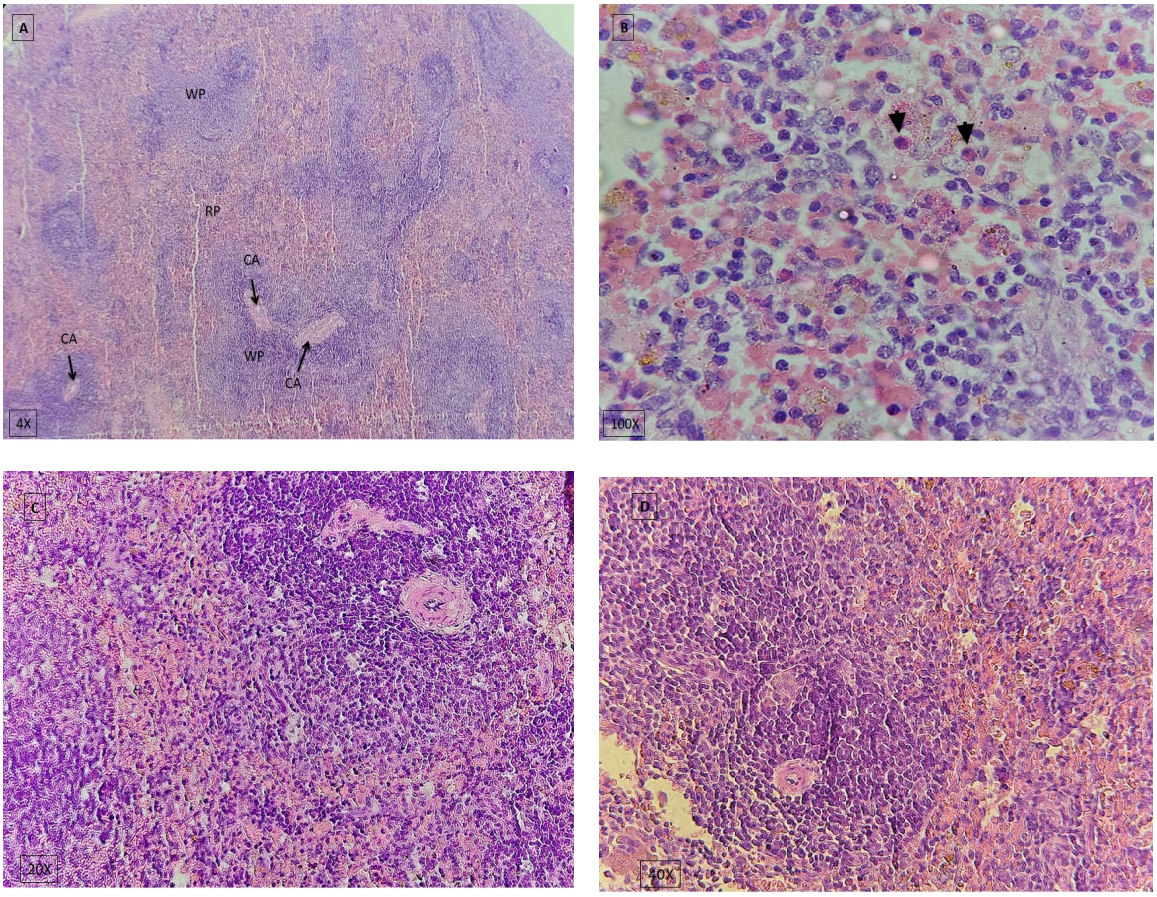

Figure (10) The histological spleen examination of the rabbit group with Cisplatin and juice of carrot. Representative images of the spleen sections demonstrated the different magnification. Panel (A) 4X. panel (B) 100x (arrow head) GRA neutrophils.

3.3 Discussion:

Generally, Cisplatin was used to treat several types of solid tumors as the most effective anticancer drug. Notwithstanding its wide use as a successful chemotherapeutic agent, it causes undesirable adverse effects, including nephrotoxicity and immunotoxicity. Toxicity, which prompts inhibition of the immune response, is considered one of the negative effects of many cytotoxic chemotherapy treatments on immunity. Cisplatin is considered to be the most widely utilized and potent effective agent for anti-cancer that causes toxicity in some vital organs in the body, such as the liver, kidneys, and heart. Cisplatin's toxic effects are due to some influences, including its capacity to affect the response of host immunity, oxidize cell membranes, damage DNA, cause mitochondrial dysfunction, and inhibit protein synthesis (Jordan and Carmo-Fonseca 2000).

Several hematological toxicities can occur during cancer therapy. In this study, changes in the hematological parameters of male rabbits treated with cisplatin and cisplatin treated with oral fresh carrot juice were investigated. Rabbits were injected intraperitoneally with 50 mg/50 ml and 5 mg/kg I.P. and administered to 3 groups of rabbits as negative-control groups and positive with cisplatin and, cisplatin-treated with oral fresh-carrot juice.

Carrot (Daucus carota) contains phytochemicals, e.g, phenols and carotenoids, that assist in decreasing the danger of cancer and disease of cardiovascular since they have anti-oxidant, anti-inflammatory, plasma lipid-modulating, and antitumor properties. Polyphenols have a role in the inhibition of progressive diseases, for instance, tumors, diseases of cardiovascular, and neurodegenerative disorders. The fresh juice of carrots contains glutathione, which is an antioxidant that defends the free radicals. It is considered an anti-inflammatory that relieves the symptoms of arthritis (Metzger *et al*., 2008).

This current study shows there was an important decrease in WBC and platelet count when compared between the group treated with cisplatin and the juice of fresh carrot plus cisplatin treated rabbits with the group of negative control. But when comparing WBCs count and platelet count between the group treated with cisplatin and group treated with juice of fresh carrot and cisplatin treated rabbits, there were no differences in WBCs count. Moreover, there were decreases in LYM and MID counts that were non-significant in the serum of rabbits treated with cisplatin paralleled to the group of negative control.

The results in the current study agree with the results documented by the study of Khalaf *et al*., (2019), which reported that clear suppression of cellular immunity due to cisplatin was shown via an important reduction in the leukocytic count, the percentage of lymphocytes, and the activity of phagocytic cells with a clear increase in neutrophil percentage. Moreover, these results in this study were observed in research via Awadallah *et al*., (2021) who indicated that IP injection of cisplatin into adult male rabbits resulted in a reduction in the WBCs count, lymphocyte count, and an increase in neutrophil count, as well as decreases in the RBCs count; contents of haemoglobin, values of haematocrit, and level of iron in the plasma, accompanied by an increase in total bilirubin. Furthermore, these results were also supported by Park *et al*., (2014) who revealed that cyclophosphamide used to treat different cancers has effects such as hematopoietic dysfunction, which reveals a decreased WBC count or leukopenia, a lower lymphocyte count, anemia, and thrombocytopenia. Furthermore, the results of this current research assist earlier findings which showed a reduction in antibody titers and a clear reduction and degeneration of lymphoid tissue by histopathological investigation of the rat spleen treated with cisplatin (Khalaf *et al*., 2019).

In this study, fresh Daucus carota L. juice was given to assess its role against the toxicity of cisplatin drug. When rabbits are given orally the juice of a fresh carrot with 5mL/kg body-weight for 4 days following earlier cisplatin injection, and 3 days following later cisplatin injection, this resulted in a slight rise in lymphocyte count and decreased GAR count, as well as a decreased level of C3, leading to the return of their count being the same as negative control. The complement compound C3 is an important protein in immunity that shows a crucial role in complement activation, and it is a vital mediator of inflammation, revealed to be essential in numerous types of tumors (Reis *et al*., 2018). The protein of cascade C3 in the complement is the predecessor of C3a and C5a, which are strong chemo attractants of cells.

It has been shown that cisplatin treatment in mice at a low-dose leads to harm to erythrocytes and causes amasses in the RP of the spleen with disturbed recycling of ferroportin and ferritin protein. This leads to increasing splenic iron content in the splenocytes and also causes specific splenic hemosiderin deposition in spleen tissue (Wang Y *et al*, 2010). It was also suggested that the treatment with cisplatin induced splenic injury and hemosiderin deposition and was not linked to the improvement of ascites tumors (Wang Y *et al*, 2010).

Cisplatin caused splenic tissue damage, as is obvious from the histological analysis of the spleen. By histological analysis of the spleen shows that cisplatin treatment (5mg/kg body-weight) in male rabbits induced significant changes in the structure of the spleen and of splenic tissue sections. The change in the white pulp and margin zone is the most significant.

Cisplatin causes many harmless and unhealthy impacts, including many toxic effects on immunity. In the current research, cisplatin given to male rabbits showed significant toxic adverse effects represented by a decreased count of all white blood cells, lymphocyte count, and platelet count in the blood.

Cytotoxic drugs affect the immune system by suppressing the immune response, which leads to a decrease in the host's resistance to both infectious agents and cancer cells. (Descotes 2006). It has been described that the cisplatin drug has an important toxic effect on the spleen (Crăciun and Paşca 2014). Immunotoxicity may be changes in a typical histological microscopic structure or size of lymphoid tissues (Pearse et al., 2009). Splenic immunosuppression may show decreased numbers of lymphocytes in the spleen or other immune tissues (Pearse *et al*., 2009), Monfared *et al*., 2014).

Cisplatin help to increase free radicals levels, especially reactive oxygen species (ROS) resulting in death of the cells. The imbalance in the generation of ROS can cause the development of oxidative stress. Oxidative stress is a mechanism that is involved in the toxicity of cisplatin. The main goal for cisplatin-prompted oxidative stress is the mitochondrion, leading to loss of the group of sulfhydrl protein of mitochondrial, inhibition of calcium absorption, and a reduction in the potential of mitochondrial membrane. The reduction in death of the cells, Mitochondria damage lead to tubular cell disorder and dying. (Saad *et al*., 2004).

In addition, it has been shown that cisplatin leads to the secrete of TNF-α one of the proinflammatory cytokines. The expression of TNF-alpha gradually increased in the tissue of spleen from 24 to 72 hours after exposure to cisplatin with a dose of 20 Mg/Kg of body-weight. However, the significant expression of TNF-α cytokine that exposure to cisplatin needs 96 hours with a amount of 10 mg/kg body-weight (Los *et al*., 1995 Moreover, a study by Banerjee *et al*., (2018) shows apoptosis occurs in spleen cells and that exposure to cisplatin activates the outer pathway of apoptosis. Moreover, the morphology and histopathology of the spleen show that cisplatin causes damage to splenic tissue. Additionally, cisplatin causes the amassing of reactive oxygen species (ROS) in the tissue of the spleen, and this production of ROS causes oxidative-stress through reducing the antioxidant catalase expression. This study has produced evidence of the important role played by fresh carrot juice against cisplatin toxicity in the spleen and some blood parameters in rabbits. The carrots with cisplatin management prompted some improvement in changes of the histo-pathological of the spleen rabbits treated. This experimental observation effect might be because of the antioxidant properties of different components.

4.0 Conclusions

In conclusion, this present study showed that treatment with cisplatin prompted immune changes in rabbits. The treatment orally with juice of a fresh carrot at dose 5ml/ kg show a

role effect against cisplatin-prompted immune-toxicity avoiding histo-pathological changes. However, further study and examination are necessary to comprehend the potential role of carrots as an assistant treatment with cisplatin

5.0 References

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