THE ROLE OF DIFFERENT CONCENTRATIONS OF COLOSTRUM SOME IMMUNOLOGICAL PARAMETERS IN MALE RATS IMMUNOSUPPRESSED

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Abstract: Present value of colostrum in this current experiment, the animals divided into one another, is a good value in this experiment (45). The group of animals that were injected with cisplatin at a concentration (2 mg/kg) and the second treatment ((T2) A group of animals that were injected with cisplatin at a concentration (2 mg/kg) and dosed with colium at a concentration (2 mg/kg)) A group of animals that were injected with cisplatin Concentration (2 mg/kg) the group of animals that were injected with the drug 500) and the third treatment (T3) The group of animals that were injected with cisplatin at a concentration of (2 mg/kg) and dosed with colostrum at a concentration of (1000) and the fourth treatment (T4) the group of animals that were injected with cisplatin at a concentration of (The group of animals dosed with cholesterol at a concentration of (500 mg/kg) and the sixth treatment (T6) and the fifth treatment (T5) The group of animals that were dosed with cholesterol at a concentration (1000 mg/kg) and the seventh factor (T7) The group of animals that were dosed with cholesterol (1500 mg/kg), after it was lowered in the excellent study in the first treatment (T1) when compared with the control and the rest of the groups, while the number of blood platelets witnessed a significant decrease (P> 0.05) when compared with the control, as it was noted A clear improvement in the values The studied treatments in treatments (T2, T3, and T4) were observed, dosed with the drug and tipped with colostrum, where the concentrations of interleukin-12, tumor necrosis factor-alpha and CIF-reactive protein were significantly (P < 0.05) compared with the second treatment (T2) (T5, T6 and T7). An increase (< 0.05) did not reach the degree of significance compared with the studied control and laws. The results also showed a significant decrease (P < 0.05) in the average number of white blood cells and the percentage of neutrophils in the first treatment, while the treatments (T2, T3 and T4) Significant increase (P> 0.05) compared with the first treatment and decreased significantly (P < 0.05) compared with the gradient, as the statistical analysis showed, a significant increase (P> 0.05) in the percentage of lymphocytic, monocytic and eosinophilic percentage compared with Taq and its ratio reports with the treatments The drug (T2, T3, and T4) with low concentration ratios, and from this we conclude the important role of colostrum in reducing the damage caused by the drug.

Keywords: colostrum, Cisplatin, immunity

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INTRODUCTION

A food supplement is a substance that is added to the diet by increasing the amount of incoming nutrients and delivering them to the need and the natural limit for them. The goal of a nutritional supplement is to provide nutrients that include vitamins, minerals, and other lesser known substances such as herbs, amino acids, enzymes, and herbal extracts. Food supplements are marketed in various forms such as tablets and softgels (Tayyem, 2018. Dietary supplements are taken for various reasons, either to build Good health or to compensate for vitamin deficiencies Examples of nutritional supplements are products such as protein, vitamins, minerals or in the diet, all of which offer advantages and disadvantages (Devla et al., 2011).

Colostrum is the first secretion of the mammary gland produced after birth, and differs from mature milk because it contains a higher concentration of proteins, immunoglobulins, vitamins, minerals (lactoferrin, lysozyme, lactoperoxidase) and growth factors. The use of bovine colostrum for human consumption has been recorded for many years in food and in medicinal treatments. Several studies have been conducted with the aim of evaluating its benefits in human dietary supplements. The results indicate an improvement in cases of gastrointestinal, respiratory, inflammatory, and bone growth diseases. It is currently marketed or online in some countries. However, its marketing for human consumption in many countries is very recent, making cholesteum a new functional food option for consumers (Silva et al., 2019).

Cisplatin (Cl2H6N2Pt) is a potent platinum-based drug used to treat many diseases related to many types of cancers in different tissues (Nasiri et al., 2020; Riddell, 2018) This drug has serious side effects that require specific precautionary measures during its use in hospitals (Roila et al., 2016), and is still the first drug used in the treatment of many types of cancer (Furue, 1985).

Cisplatin toxicity is due to cross-linking within and between nuclear strands, causing various effects, including several pathologies of nephrotoxicity, hepatotoxicity, cardiotoxicity,

thrombocytopenia, anemia, and peripheral nervous system dysfunction (Dilruba and Kalayda, 2016). Although the mechanism of toxicity of cisplatin in body tissues is fully understood, effective treatment and prophylaxis to reduce these changes are missing. Therefore, there is a need to develop a substance to secure the use of cisplatin (Sun et al., 2019 Qian-Yu). Recent studies tend to use potent natural plant-based antioxidants and nutritional supplements to prevent or reduce oxidative stress and inflammation caused by cisplatin use that have shown excellent effects on the pathophysiological status (Crona et al., 2017; Abdel-Daim et al., 2019).

MATERIALS AND METHODS

Experimental animals

The study was conducted in the animal house of the College of Education / University of Al-Qadisiyah, under standard conditions of temperature (22-28°C), ventilation and illumination period (14 hours of light and 10 hours of darkness). The animals were given free feeding and water for the duration of the experiment.

Experimental design

The experiment included 45 male rats distributed into (8) groups, each group included 5 animals for a period of 21 days as follows:

1- Control group (C): the group of animals that were dosed with normal saline physiological solution for 21 days.
2- First treatment (T1): the group of animals that were injected with cisplatin at a concentration (2 mg/kg of body weight) under the peritoneum once a week for 21 days.
3- The second treatment (T2): a group of animals that were injected with cisplatin at a concentration of (2 mg/kg) of body weight once a week, then they were dosed with colostrum at a concentration of (500) daily for a period of 21 days.
4- The third treatment (T3): a group of animals that were injected with cisplatin at a concentration of (2 mg/kg) of body weight once a week, then they were dosed with colostrum at a concentration of (1000) daily for a period of 21 days.
5- Fourth treatment (T4): a group of animals that were injected with cisplatin at a concentration of (2 mg/kg) of body weight once a week, then they were dosed with colostrum at a concentration of (1500) daily for a period of 21 days.
6- The fifth treatment ((T5): the group of animals that were dosed with cholesterol at a concentration of (500 mg/kg) of body weight daily for 21 days.
7- The sixth treatment (T6): a group of animals that were dosed with cholesterol at a concentration of (1000 mg/kg) of body weight daily for a period of 21 days.
8- The seventh treatment ((T7): the group of animals that were dosed with cholesterol at a concentration of (1500 mg/kg) of body weight per day for 21 days.

Cisplatin Dosage

Cisplatin was obtained from drug stores in the form of a liquid bottle with a concentration of 50 mg / 100 ml and the dose was prepared as described (Richardson and Gangolli, 1993) at a concentration of 2 mg / kg of body weight by dissolving the required concentration depending on the average body weight of the animal and each animal was injected Weekly under the peritoneum for 21 days.

Interleukin-12

The level of interleukin-12 in the serum was determined using the ELISA test and by the Direct ELISA Sandwich method according to the instructions contained in the examination kit supplied by the Chinese company BT Lab.

C-reactive protein concentration

The CRB-Latex assay is a rapid-slide stacking assay based on a modification of the latex fixation method, and was developed for the direct detection of C-reactive protein (CRP) and its semi-quantitative determination in serum according to (Singer and Plotz, 1956) method.

Platelets, total and differential numbers of white blood cells

It was examined using a device (Auto Blood Analyzer Sysmex-XP300), by placing a sample of blood drawn in.Then all the results for the above criteria were recorded directly from the device.

Molecular analysis

Quantitative real-time polymerase chain reaction (reverse cloning) assay.

The reverse transcription polymerase chain reaction assay was performed to measure the quantitative levels of mRNA to indicate the amount of TNFα gene expression, and GAPDH gene was used as a standard regulator gene for calculating gene expression.

Statistical analysis

After data collection and tabulation, statistical analysis program SPSS V.25 was used. Where the data were statistically analyzed according to the one-way ANOVA test, and the averages of the experiment groups were compared when the differences between them were significant using the Least Significant Difference (LSD) test at the level of significance 0.05 (Al-Rawi and Khalaf Allah, 2000).

RESULTS AND DISCUSSION

The results of the statistical analysis shown in Table (1) showed a significant ($P<0.05$) increase in the concentration of interleukin-12 in the first treatment (T1) compared with the control and other treatments, and the fourth treatment (T4) saw a significant ($P<0.05$) decrease in the IL level. -12 compared with (T1), and there was no significant difference ($P<0.05$) between them and between the second treatment (T2) and the third treatment (T3), and the statistical analysis showed a significant decrease ($P<0.05$) in the level of IL-12 in the fifth treatments. (T5), sixth (T6) and seventh (T7) treatment when compared with the first treatment (T1), and no significant differences ($0.05<P$) were observed between them and the control.

The results of the statistical analysis also showed a significant ($P < 0.05$) increase in the TNF concentration rate in the first treatment (T1) compared to the control and other treatments, while the third treatment (T3) and the fourth treatment (T4) experienced a significant decrease ($P < 0.05$) compared to treatment. With treatment (T1) and no significant ($0.05<P$) differences when comparing them with the control, and the statistical analysis showed a significant decrease ($P<0.05$) in

TNF-alpha in the fifth treatment (T5) and the sixth treatment (T6) and the treatment The seventh (T7) when compared with the first treatment (T1) that was immunosuppressed, and the results agreed with (Acar et al., 2020).

Chemotherapy is described as an anti-cancer chemotherapy drug called cytotoxic therapy, which destroys fast-growing cancer cells and stops their growth and division, and chemotherapy disrupts the process of cancer cell division and elimination (Akca et al., 2018) and the high level of TNF-α is caused by damage What happened in the liver, as the results of the current study showed a decrease in the functional capacity of the liver depending on the values of its functions, if the liver is unable to remove the high levels of cellular kinetics, and the reason for the rise of TNF-α is due to the high levels of enzymes AST, ALP, ALT, as Between (Guobin and Michael, 2011) that reducing TNF-αR receptors will reduce the damage to hepatocytes significantly, and the high concentration of TNF-α will increase the necrosis of hepatocytes and increase the release of its enzymes into the bloodstream.

IL-12 is the most powerful antitumor cytokine as it stimulates natural killer cells, enhances CTL maturation, and also induces the production of IFN which has a role as an effective molecule to initiate the Th1 response (Ullrich et al., 2020), and IL-12 inhibits Th2 cells and their cytokine production. (Billerbeck et al., 2014) Elevated levels of TNF-α and IL-12 in animals treated with anticancer chemotherapy are evidence of tissue damage, tumorigenesis, and inflammation in organ cells (Raetska et al., 2017);Uzrail et al., 2019) . Colostrum coordinates the immune balance and reduces the inflammatory response by increasing the proliferation of CD4 and CD8 cells and modulating the immunosuppressive pathways. The lactoferrin present in colostrum reduces inflammatory factors and plays a protective role to protect tissues from damage as it reduces interleukin and inhibits tumor necrosis factor (Machnicki). et al., 1993; Ghosh and Iacucci, 2021)

The results of the statistical analysis also showed a significant decrease ($P < 0.05$) in the number of platelets in the first treatment (T1) compared with the control and other treatments, while the second treatment (T2), the third treatment (T3) and the fourth treatment (T4) saw a significant increase (<0.05). P) in the number of platelets in comparison with the first treatment (T1) and a significant decrease (0.05<P) in comparison with the control, and the statistical analysis showed a significant increase (P<0.05) in the number of platelets in the fifth treatment (T5) and the sixth treatment (T6).) and the seventh treatment (T7) when compared with the first treatment (T1) which was immunosuppressed. I agree with (Noviyani et al., 2019). The reason for the decrease is attributed to the fact that cisplatin binds directly to the DNA of bone marrow cells, which causes damage to DNA during its replication (Perry, 2008) and thus leads to a decrease in the number of platelets in white cells (Wilson et al., 2007). Colostrum contains growth factors that activate the bone marrow immediately after absorption into the bloodstream. It also contains proteins that indirectly stimulate dendritic cells by activating innate immunity (Davis et al., 2007) (Tokuyama et al., 1990;). The major colostrum protein lactoferrin, along with other colostrum components, has been shown to play an important role in promoting myelogenesis. When taken orally, it also has an effect on reducing tissue damage and lowering the level of inflammation (Artym and Zimecki, 2007; Choi et al., 2010), and colostrum stimulates bone marrow progenitor cells, which in turn increases platelet formation (Webster and Lehrke, 2013), and the use of high concentrations of cholesteatoma does not cause an abnormal increase in platelets because it does not cause any damage to the bone marrow, and this is what our results proved and confirmed (Pourliotis et al., 2012).

The results of the statistical analysis showed a significant ($P < 0.05$) increase in C-reactive protein in the first treatment (T1) compared with the control and other treatments, while the second treatment (T2), the third treatment (T3) and the fourth treatment (T4) saw a significant decrease (0.05). <P) in C-reactive protein when compared with treatment (T1), and the fifth treatment (T5), the sixth treatment (T6) and the seventh treatment (T7) showed a significant decrease (P> 0.05) when compared with the first treatment (T1) and the results agreed with both From a study (Erbas et al., 2014), the reason is due to the strong toxicity of the chemical drug, as it caused an increase in the tumor necrosis factor (TNF-α) and caused the destruction of body tissues and increased inflammation, which is evidence of increased inflammation (Ahmad et al., 2019), the role of cholesterol It is evident in lowering the level of both CRP and that it has beneficial health effects that can be CRP and TNF-α intake in mice reduce the rate of tumor growth by decreasing pro-inflammatory cytokines (Badkook et al., 2013). CRP is a major acute phase protein, primarily expressed and secreted by hepatocytes in response Cytokines such as IL-6 under inflammatory conditions, 2011; Ingle and Patel, and thus the improvement is achieved as it protects and protects the liver and this is proven by the results of our study and contributed to reducing inflammation as a result of it containing sugars of the type oligosaccharides that reduce inflammation in the intestines and colon (Martinez et al., 2006; Daddaoua et al., 2006) as well as the rest of the ingredients, including vitamin E, which is a powerful antioxidant that provided protection for the liver and kidneys and reduced inflammation (Asbaghi et al., 2020; EFSA, 2015). Thus, a clear improvement was observed in the treatments. and lower CRP.

Table 1. shows the effect of different concentrations of colostrum on the immune parameters in rats immunosuppressed with cisplatin.

group standards	IL-12 pg/ml))	tumor necrosis factor alpha pg/ml)))	platelet count (x103/mm)	C-reactive protein (mg/L)
C	6.28 ±0.88 C	1.34±0.16 B	341.80±2.31 A	7.06±0.03 E
T1	11.63±1.10 A	3.36±0.68 A	263.40±4.22 E	8.27±0.07 A
T2	10.10±0.84 AB	2.34±0.45 AB	298.60±3.68 D	7.95±0.04 B
T3	9.53±1.31 B	1.95±0.37 B	315.00±3.28 C	7.68±0.04 C

T4	9.43±0.53 B	1.50±0.28 B	330.00±2.54 B	7.32±0.04 D
T5	7.14±0.69 C	1.38±0.20 B	338.60±2.83 AB	7.06±0.03 E
T6	7.45±1.09 C	1.37±0.26 B	334.80±3.80 AB	7.12±0.04 E
T7	7.79±0.85 C	1.38±o.22 B	330.20±3.05 B	7.17±0.32 E
LSD	2.01	1.06	9.44	0.135

*Different letters indicate significant differences between the treatments ($P < 0.05$).
* Similar letters indicate that there are no significant differences between the treatments ($0.05<P$).
C: Same as the control group that dosed physiological saline for the duration of the experiment (21 days).
T1: The first treatment represents a group of rats that were immunosuppressed with cisplatin mg/kg bw.
T2: The second treatment represented a group of rats that were immunosuppressed and dosed with colostrum at a concentration of 500 mg/kg of body weight.
T3: The third treatment represents a group of rats that were immunosuppressed and dosed with colostrum at a concentration of 1000 mg/kg body weight.
T4: The fourth treatment represents a group of rats that were immunosuppressed and dosed with colostrum at a concentration of 1500 mg/kg of body weight.
T5: The fifth treatment represents the group of rats fed with colostrum at a concentration of 500 mg/kg body weight.
T6: The fifth treatment represents the group of rats fed with colostrum at a concentration of 1000 mg/kg body weight.
T7: The fifth treatment represents the group of rats with colostrum at a concentration of 1500 mg/kg body weight

The results of the statistical analysis shown in Table (2) showed a significant decrease ($P<0.05$) in the total number of white blood cells in the first treatment (T1) compared with the control and other treatments, while the second treatment (T2), the third treatment (T3) and the fourth treatment experienced (T4) a significant increase ($P<0.05$) in the total number of white blood cells in comparison with the first treatment (T1) and a significant decrease ($P<0.05$) in comparison with the control. It is noted that the fourth treatment (T4) increased significantly ($P<0.05$) compared with The second transaction (T2) and the third transaction (T3).

The results of the statistical analysis showed a significant ($P<0.05$) increase in the average number of lymphocytes in the first treatment (T1) compared with the control and other treatments, except for the second treatment (T2) and the third treatment (T3), which did not witness significant differences ($P>0.05$). Compared with the first treatment (T1) and it increased significantly compared with the control ($P<0.05$), while the fourth treatment (T4) decreased significantly ($P<0.05$) compared with the first treatment (T1) and no significant difference was observed ($P>0.05$) compared to the control .

A significant decrease ($P<0.05$) was also observed in the average percentage of neutrophil count in the first treatment (T1) compared with the control and other treatments, while the second treatment (T2), the third treatment (T3) and the fourth treatment (T4) saw a significant increase (P). < 0.05) in neutrophils compared to the first treatment (T1) and decreased significantly ($P<0.05$) in comparison with the control, and the statistical analysis showed a significant increase ($P<0.05$) in the average number of neutrophils in the fifth treatment (T5) and the sixth treatment (T6) and the seventh treatment (T7) when compared with the first treatment (T1), the second treatment (T2), the third treatment (T3) and the fourth treatment (T4) that were immunosuppressed and at the same time no significant difference ($P>0.05$) was observed between them and the control.

The results of the statistical analysis also showed a significant increase ($P<0.05$) in the average number of mononuclear cells in the first treatment (T1) compared with the control and other treatments except for the second treatment (T2) and the fifth treatment (T5) that converged with it, while the third treatment (T3) witnessed) And the fourth treatment (T4) had a significant decrease ($P<0.05$) in the average number of mononuclear cells compared with (T1), and it had increased significantly ($P<0.05$) when compared to the control.

The results of the statistical analysis showed a significant ($P<0.05$) increase in the average number of eosinophils in the first treatment (T1) compared with the control and other treatments, while the third (T3) and the fourth (T4) showed a significant ($P<0.05$) decrease in the average number of eosinophils. The eosinophil cells compared with (T1) and a significant increase ($P<0.05$) compared to the control, and the statistical analysis showed a significant decrease ($P<0.05$) in the average number of eosinophil cells in the fifth (T5) and sixth (T6) and seventh (T7) treatments when It was compared with the first treatment (T1) which was immunosuppressed and at the same time no significant difference ($P>0.05$) was observed when compared with the control. The results agreed with each of the study (Mackall et al., 1994), which showed a significant increase ($P<0.05$) in lymphocytes, and a significant decrease also in the percentage of neutrophils for the same group mentioned above, and this is consistent with the study (Schimpff et al., 1971; Vokes, 2001) as they showed that the reason for the decline is due to the effect of chemotherapy on the bone marrow. The study also showed a significant increase ($P<0.05$) in the percentage of eosinophils and monocytes in treatment (T1), as (Shin et al., 2003)) indicated that this type of cells is responsible for the confrontation against bacterial infections and cancerous infections, as these The cells secrete cytokines of the type Monokines, the most important of which is the Tumor Necrosis Factor, and it is considered one of the anti-cancer agents, and this agrees with my study and the results of (Lysov et al., 2012; Weir et al., 2011). Cisplatin stimulates the appreciation of this type of cells, as it is one of the main

components responsible for the autoimmune response towards the process of phagocytosis, dead cells, and anti-cancer activity (Doseff and Parihar, 2012). The ratio of these cells is a normal condition in order to get rid of dead cells and confront cancerous cells.

An improvement was observed in the white and differential blood cells compared to the treated group (T1), and an improvement was noted in the treatment (T4), and this is due to the fact that colostrum contains important mineral elements such as (Zn, Cu, Fe, Mg, Mn), which caused an increase in the immune response and activation of cells. To do defense (Shah et al., 2019; Hafsan et al.,2022), and several studies showed the role of vitamin (C) present in colostrum in reducing the rate of eosinophils, and this is due to the fact that these cells increase in allergic reactions and in the case of inflammation (inflammation) and increase histamine Histamine) secreted from basal cells, against which antihistamine is secreted by eosinophils (Sharma et al., 2016; Gaby and Singh, 1991), as it is considered an Eosinophil chemotactic factor, and thus works to attract the latter to The inflamed area to detoxify some inflammatory substances (Silverthron, 1998; Huldani et al.,2022). Which was confirmed by (Clemetson, 1999), which clarified the role of the vitamin in reducing histamine and thus reducing the proportion of eosinophils and basophils in the treatment (T4, T5). It provides protection for neutrophil cells from oxidative damage to active oxygen species (ROS), which they may intercept when performing the function of phagocytosis (Sharma et al., 2004; Zadeh et al.,2022). My study is similar to the study (Samir et al., 2000) when giving vitamins to treated animals. to an improvement in hematological parameters and traceable rates are close to control.

Table 2. shows the effect of different concentrations of Colostrum on the differential number of white blood cells in rats immunosuppressed with cisplatin.

group standards	W.B.C Count	LYM (%)	NEU (%)	MONO (%)	Eosino (%)
C	9.96±0.08 A	65.99±2.16 C	25.00±1.90 A	5.29±0.25 C	3.73±0.19 D
T1	4.76±0.04 E	74.99±2.16 A	11.00±0.98 D	7.10±0.30 A	7.11±0.26 A
T2	5.76±0.19 D	72.97±1.67 AB	19.82±0.50 B	6.57±0.23 AB	6.59±0.19 A
T3	6.80±0.19 C	71.87±1.63 AB	15.11±0.99 C	6.21±0.17 B	5.72±0.16 B
T4	7.85±0.31 B	67.62±2.47 BC	18.04±0.45 C	5.38±0.15 C	4.71±0.24 C
T5	9.76±0.12 A	64.33±2.43 C	24.69±1.23 A	6.99±0.18 A	3.78±0.04 D
T6	10.01±0.05 A	66.01±2.06 C	24.44±1.13 A	5.30±0.19 C	4.25±0.15 CD
T7	10.25±0.18 A	67.95±0.59 BC	23.11±1.38 AB	5.21±0.09 C	4.22±0.35 CD
LSD	0.492	5.72	3.35	0.601	0.580

*Different letters indicate significant differences between the treatments ($P < 0.05$).

* Similar letters indicate that there are no significant differences between the treatments ($0.05<P$).

C: Same as the control group that dosed physiological saline for the duration of the experiment (21 days).

T1: The first treatment represents a group of rats that were immunosuppressed with cisplatin mg/kg bw.

T2: The second treatment represented a group of rats that were immunosuppressed and dosed with colostrum at a concentration of 500 mg/kg of body weight.

T3: The third treatment represents a group of rats that were immunosuppressed and dosed with colostrum at a concentration of 1000 mg/kg body weight.

T4: The fourth treatment represents a group of rats that were immunosuppressed and dosed with colostrum at a concentration of 1500 mg/kg of body weight.

T5: The fifth treatment represents the group of rats fed with colostrum at a concentration of 500 mg/kg body weight.

T6: The fifth treatment represents the group of rats fed with colostrum at a concentration of 1000 mg/kg body weight.

T7: The fifth treatment represents the group of rats with colostrum at a concentration of 1500 mg/kg body weight.

COMPLIANCE WITH ETHICAL STANDARDS STATEMENTS

I. Ethical approval:

The manuscript is written in original and all the data, results pertaining to this manuscript are original according to the research performed. The authors followed academic integrity and have not copied any content/results from another source.

II. Funding details (In case of Funding):

The authors of this manuscript did not receive any funding to perform the present research

III. Conflict of interest

The authors of the study do not have any conflict of interest

IV. Informed Consent:

The authors of the manuscript agrees to publish this research in the journal if it's considerable by the editors of the journal. The authors provide full consent for reviewing and publishing this manuscript.

V. All the authors of this study contributed equally in terms of performing the research as well as in preparing the manuscript. All the authors of the study followed the guidelines of the corresponding author. Any query/suggestion related to the manuscript can be reached to the corresponding author

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