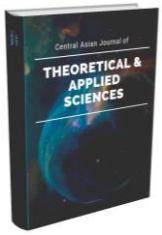

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Article

The Negative Effect Of Cisplatine On The Reproductive System Of Albino Rats And The Preventive Role Of Silybum Marianum Seed Extract And Vitamin C

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Abstract: This study aims to test the efficacy of Silybum marianum and vitamin C against CP toxicity on hormone secretion and testicular function in sperm production. Thirty male albino mice aged between (98-112) days were used. The animals were divided into (6 groups) (five per group) and the animals were treated with cisplatin, vitamin C and alcoholic extract of Silybum marianum for one month as follows: control group (i) animals given distilled water (1 ml), infected group (ii) injected with CP at a concentration of (2 mg/kg) subperitoneally once a week, group (iii) injected with vitamin C at a concentration of (100 mg/kg), group (iii) injected with alcoholic extract of Silybum marianum at a concentration of (200) mg/kg, group (iiii) injected subperitoneally with CP at a concentration of (2 mg/kg) weekly for 4 weeks and injected with vitamin C daily at a concentration of (100 mg/kg) at one time until the end of the experiment, group (iiii) injected subperitoneally with CP at a concentration of (2 mg/kg) were given a dose of alcoholic extract of Silybum marianum At a concentration of (200 mg/kg) daily at the same time weekly for 4 weeks until the end of the experiment. After the end of the dose period, the rats were anesthetized, then blood was drawn by cardiac stab and placed in a gel tube and placed in a centrifuge for 20 minutes / 5000 rpm. The serum was stored at a temperature of 20 °C in an Eppendorf tube until the date of testing the hormones LH, FSH and testosterone. After that, the animals were dissected, the testicles were removed and placed in formalin (10%) for fixation for three days, then washed with water and stored in 70% alcohol. The results showed the following: Figure 1, 2, 3 show that the CP-treated group showed a significant decrease in the concentration of LH, FST and testosterone hormones compared to the healthy group, while treatment with vitamin C, treatment with Silybum marianum alcoholic extract, treatment with vitamin C and cisplatin, treatment with Silybum marianum alcoholic extract and CP led to a significant increase in the concentration of LH, FST and testosterone hormones compared to the control group. The results of the histological sections of the testicles showed the presence of colloidal material inside the tubules and incomplete maturation of spermatozoa in the cisplatin-treated group. In the vitamin C-treated group and the Silybum marianum extract-treated group, the seminiferous tubules appeared normal and the stages of spermatogenesis were observed with the observation of Leydig cells. Histological sections of the CP and vitamin C treated group and the CP and Silybum marianum extract treated group showed that the seminiferous tubules were in normal shape, and the stages of spermatogenesis were observed, with Leydig cells observed.

Keywords: Cisplatin , Silybum marianum , Vit C , testosterone , LH; FSH

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1. Introduction

Cisplatin (CP) is an effective platinum-containing drug used to treat many diseases related to several types of cancer in different tissues (Nasiri et al., 2020). This drug has serious side effects that require specific preventive measures during its use in hospitals. There is a side effect related to the use of (CP) in cancer patients, such as vomiting, nausea, temporary hair loss, diarrhea, and general dehydration, in addition to the appearance of many cellular, tissue, and blood effects. The toxicity of (CP) is attributed to the cross-linking between and within nuclear threads, which causes various effects, including many diseases of liver toxicity, kidney toxicity, cardiac toxicity, anemia, thrombocytopenia, and dysfunction of the peripheral nervous system (Digby et al., 2020). Its toxic effect is represented by programmed cell death (Apoptosis), oxidative stress, necrosis, and inflammation (Manohar and Leuug,2018). Despite understanding the toxic mechanism, (CP) in the tissue, but the effect of effective treatment and preventive material to reduce these changes remains neglected, so a material must be developed to ensure the use of (CP) (Sun et al ., 2019). Recent studies tend to use effective natural plant antioxidants and nutritional supplements to prevent or reduce inflammation and oxidative stress resulting from the use of the drug (CP), which in turn showed important effects on the pathological physiological condition (Abdel-Daim et al., 2019). Researchers interested in nutrition have studied the effect of a number of medicinal plants to achieve better performance in animals, including the wild milk thistle or Silybum Marianum, which belongs to the Carduus Marianum family. Its medicinal extracts have been used as anti-inflammatory, antioxidant, anti-cancer, and anti-diabetic (Zhang et al., 2020, Bielski, 2021). Its seeds are used for liver diseases and to protect it from toxins, because the chemicals it contains are effective in treating liver disorders and cholecystitis, in addition to being considered a stimulant for the production of antibodies. (Elateeeq et al., 2020).

The seeds of the Kalgan plant contain silymarin, which consists of five main components: silychristin, silybin, isosilybin, taxifolin, and silydiain. Silymarin works in four different pathways as a cofactor in regulating glutathione within cells, enhancing the production of RNA in the cell, an antioxidant, and as a stabilizing and regulating factor for cell membrane permeability that prevents the entry of foreign substances into liver cells. Kalgan works significantly to reduce cholesterol and triglyceride levels in plasma (Marmouzi et al ., 2021).Vit C is a powerful antioxidant, anti-inflammatory, immunomodulator, and cofactor for essential monooxygenase and dioxygenase enzymes (Spoelstra et al .,2018). As a result, Vit C shows a multidirectional effect (Carita et al., 2020). Various studies have shown that Vit C has hepatoprotective properties, and this effect is due to its strong antioxidant properties. This has been investigated in vitro and in vivo, i.e. studies conducted on the living body. A study conducted on liver injury indicated that Vit C normalizes the following enzymes, including aminotransferase ALT, alkaline phosphatase ALP, aspartate aminotransferase AST, and malondialdehyde (MAD) (He et al., 2018). Therefore, Vit C is an antioxidant that works to reduce most of the reactive oxygen species that are constantly formed in the cells and tissues of the body in order to get rid of their harmful oxidative effects. Vit C helps protect the body against cardiovascular diseases, cataracts, and aging.(Da Cruz et al., 2018). It has a role in the development and regulation of cancer growth and slowing down tumor growth. In case of its deficiency, it leads to scurvy disease (Klimant et al., 2018).Vit C deficiency occurs in neutrophil cells in the tumor area (Xi, 2019). In case of Vit C depletion, tissue disintegration occurs with the dissolution of the basic substance between cells and the tearing of collagen. The effect of Vit C treatment in cancer patients depends on the method of taking it, the ability of cancer cells to absorb, and the plasma concentration (Chong et al., 2019). Vit C plays a role in the efficiency of humoral and cellular immunity, which makes it play a role in the anti-cancer immune response (Magri et al., 2020).

2. Materials and Methods

The research study was conducted on 30 male white rats, aged between fourteen and fifteen weeks and weighing between (200-260) grams, and they were randomly divided into (6) groups (5 rats in each group). The rats were treated with cisplatin, vitamin C and alcoholic extract of Silybum marianum for four weeks as follows:

1) Control group Animals given distilled water (1 ml).
2) The infected group that was injected with cisplatin (CP) at a concentration of (2) mg/kg, subperitoneally once a week.
3) The group that was dosed orally with Vitamin C (Vit C) at a concentration of (100 mg/kg).
4) The group that was orally dosed with the alcoholic extract of Silybum marianum at a concentration of (200) mg/kg of body weight.
5) The group that was subperitoneally injected with CP at a concentration of (2) mg/kg) per week for 4 weeks and dosed with Vit C daily at a concentration of (100) mg/kg simultaneously until the end of the experiment.
6) The group that was injected subperitoneally with CP at a concentration of (2) mg/kg per week for 4 weeks and was orally dosed with the alcoholic extract of Silybum marianum at a concentration of (200 mg/kg) daily simultaneously until the end of the experiment. After the experiment was completed, the animals were anesthetized with chloroform and blood was drawn by cardiac stab and placed in a gel tube and then placed in a centrifuge for 15 minutes at 3000 rpm. The serum was stored at 20°C in a Eppendorf tube until LH, FSH and testosterone hormones were analyzed. The animals were then dissected, the testes were removed and placed in formalin (10%) for fixation for 72 hours, then washed with water and stored in 70% alcohol.

3. Results

This experiment was conducted to evaluate the effectiveness of Silybum marianum and Vit C on testicular function and LH, FST and Testosterone hormones against CP toxicity after exposing rats to a concentration of (2 mg/kg) of CP by subperitoneal injection once a week for 4 weeks and then treated with Vit C and Silybum marianum alcoholic extract and the concentrations of LH, FSH and testosterone hormones were measured and the results showed the following:-

1) Biochemical variables

Figures 1, 2, 3 show that the CP-treated group showed a significant decrease in the concentration of LH, FST and Testosterone hormones compared to the healthy group, while treatment with Vit C, treatment with Silybum marianum alcoholic extract, treatment with Vitamin C and Cisplatin, treatment with Silybum marianum alcoholic extract and CP resulted in a significant increase in the concentration of LH, FST and Testosterone hormones compared to the control group.

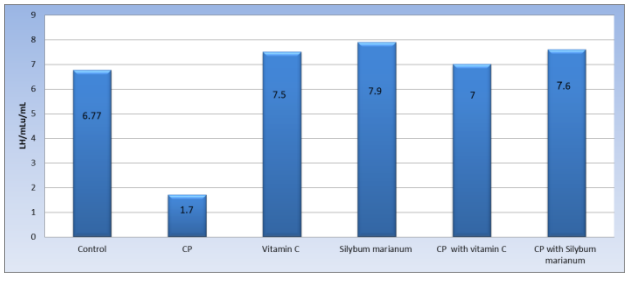

Figure 1 (shows the effect of treatment with CP at a concentrate of (2 mg/kg), treatment with vitamin C, treatment with Silybum marianum, treatment with CP and Vit C together, and treatment with CP and Silybum marianum together on the concentration of LH hormone).

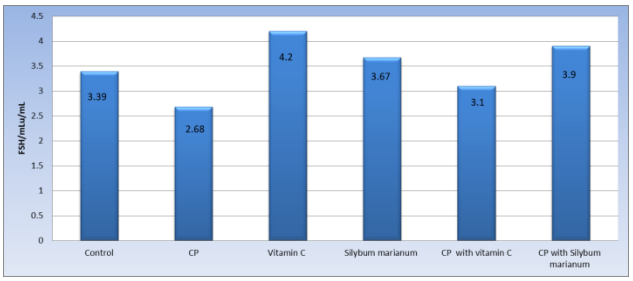

Figure 2 (shows the effect of treatment with CP at a c concentrate of (2 mg/kg), treatment with vitamin C, treatment with Silybum marianum, treatment with CP and Vit C together, and treatment with CP and Silybum marianum together on the concentration of FSH hormone).

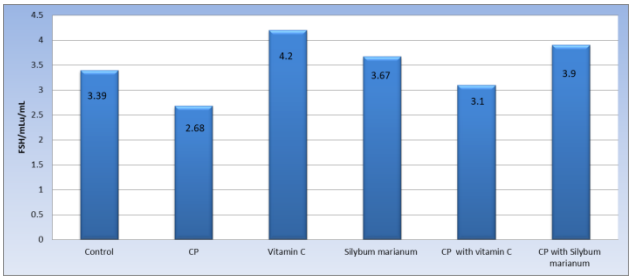

Figure 3 (shows the effect of treatment with CP at a concentrate of (2 mg/kg), treatment with vitamin C, treatment with Silybum marianum, treatment with CP and Vit C together, and treatment with CP and Silybum marianum together on the concentration of Testosterone hormone).

2) Study Histological

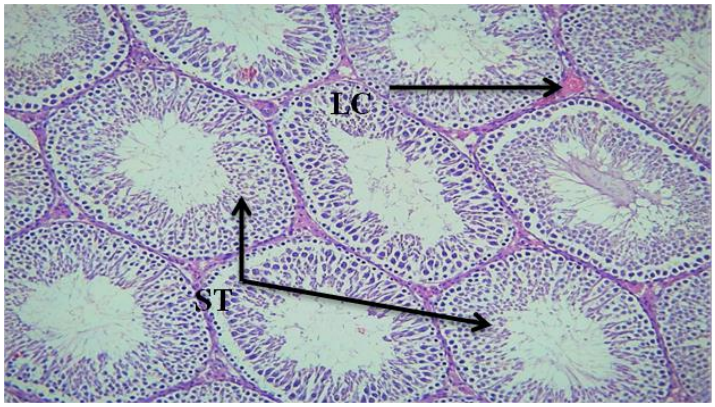

Figure (A1) a section of the testicles of the control group showing the seminiferous tubules (ST) in their normal shape, and Leydig cells (LC) can be observed. H & E 100X.

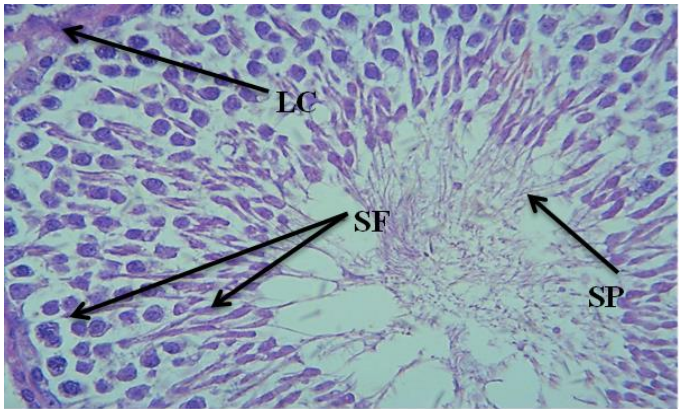

Figure (A2) A section of the testes of the control group showing the stages of spermatogenesis (SF) and mature sperm (SP). Leydig cells (LC) can also be observed. H & E 400X

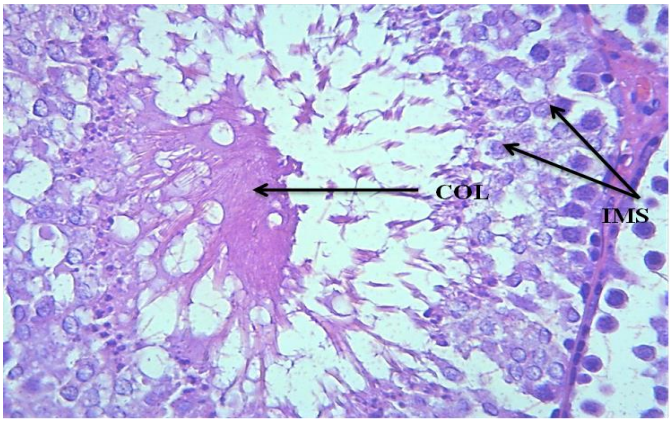

Image (B1) testicular tissue of the group treated with CP showing the presence of colloidal material inside the tubules (COL) and incomplete maturation of sperm (IMS). H & E 100X.

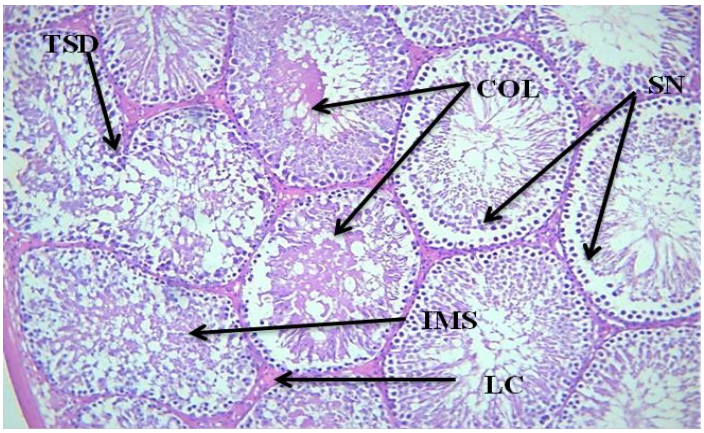

Image (B2) A section of the testicles of the group treated with CP shows the destruction of the Tubuli seminiferi (TSD), the presence of colloidal material inside the tubules (COL), and incomplete maturation of the sperm (IMS). It is also possible to observe destroyed Leydig cells (LCD) and sperm necrosis (SN). H & E 100X.

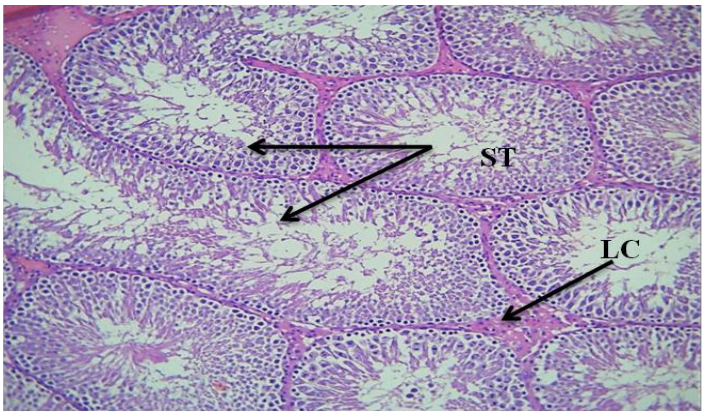

Image (C1) Transvers section of the testicles of the group working with Vit C shows the seminiferous tubules (ST) in their normal shape. The stages of sperm formation can also be observed, with the observation of Leydig cells (LC). H & E 100X.

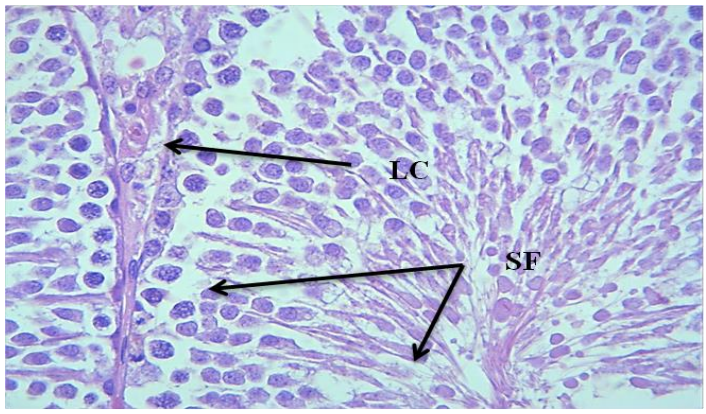

Image (C2) Crosssection of the testicles of the group working with Vit C shows the seminiferous tubules in their normal shape. The stages of sperm formation (SF) can also be observed, with the Leydig cells (LC) observed. H & E 400X.

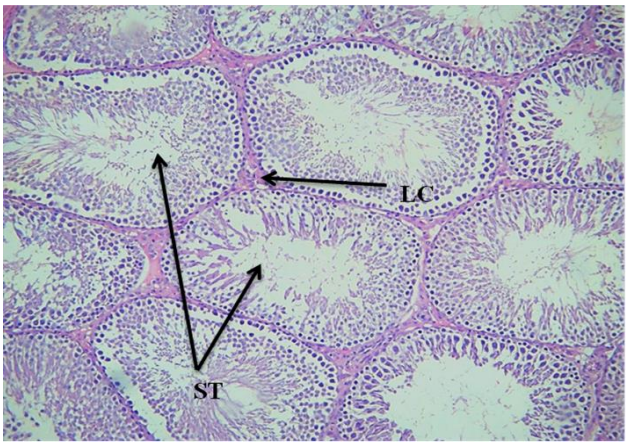

Image (D1) A section of the testicles of the group working with the extract of the Silybum marianum, showing the seminiferous tubules (ST) in their natural form. The stages of sperm formation can also be observed, with the observation of Leydig cells (LC). H & E 100X.

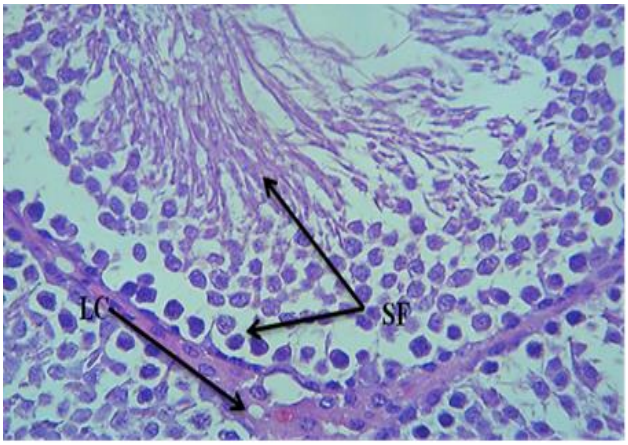

Image (D2) A section of the testicles of the group working with the extract of the Silybum marianum, showing the seminiferous tubules in their natural form. The stages of sperm formation (SF) can also be observed, with the observation of Leydig cells (LC). H & E 400X

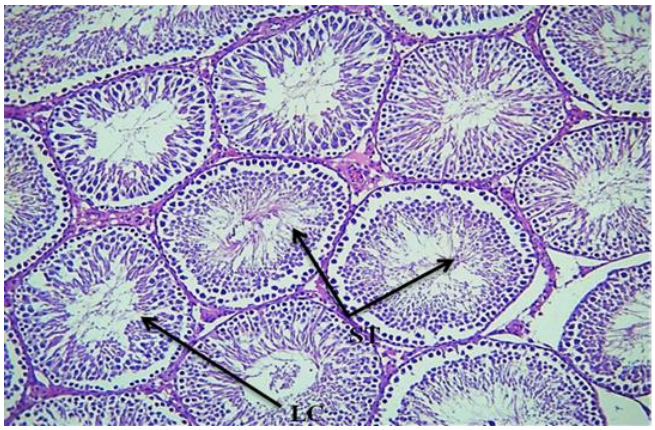

Figure (E1) Crosssection of the testes of the group treated with CP and Vitamin C, showing the seminiferous tubules (ST) in their normal shape. The stages of sperm formation can also be observed, with the Leydig cells (LC) observed. H & E 100X.

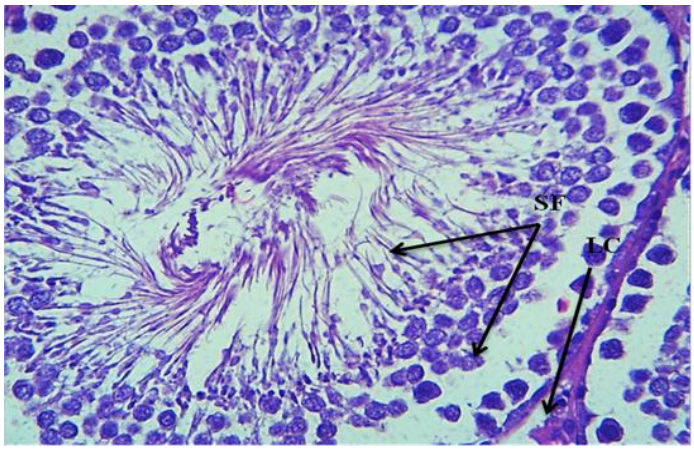

Image (E2) A section of the testicles of the group treated with CP and Vitamin C, showing the seminiferous tubules in their normal shape. The stages of sperm formation (SF) can also be observed, with Leydig cells (LC) observed. H & E 400X.

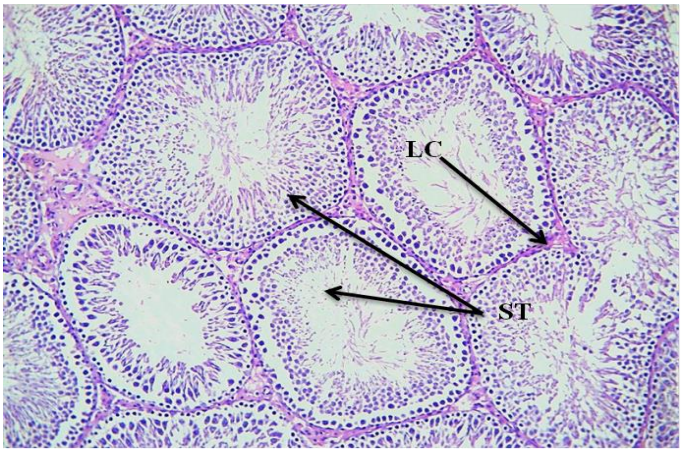

Figure (F1) Transvers section of the testes of the group treated with CP and Silybum marianum, showing the seminiferous tubules (ST) in their normal shape. The stages of sperm formation can also be observed, with Leydig cells (LC) observed. H & E 100X.

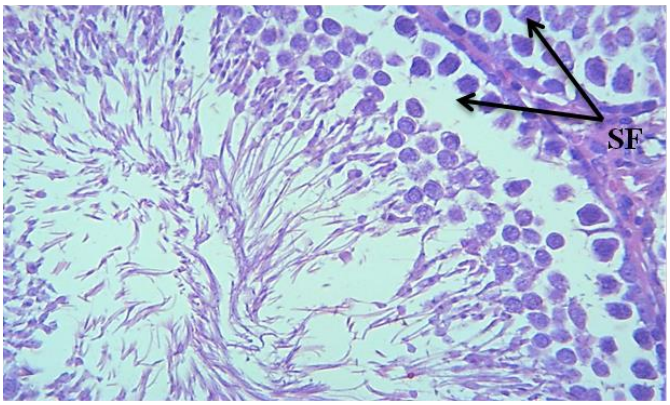

Figure (F2) A Histological section of the group treated with CP and Silybum marianum, showing the stages of sperm formation (SF). H & E 100X.

4. Discussion

The rat model provides an attractive alternative to humans for the physiological study of drugs used to treat cancer and other diseases that affect the reproductive functions of male rats. Low sperm count is an indicator of male infertility. (Adewoyin et al., 2017) We note from Figures (1, 2, 3) that the group given CP showed a significant decrease in the concentration of both LH and FST hormones and testosterone hormone in the blood serum compared to the healthy group.The growth of the male reproductive organs and the process of spermatogenesis depend on androgen. The quantity and condition of mature Leydig cells will decrease and their physiological function will decrease with the decrease in androgen production (Houda et al ., 2021 ,Ge& Wang, ., 2021). In males, FSH hormone regulates the activity of the seminiferous tubules and Sertoli cells, which in turn maintains many aspects of sperm cell maturation. It is also important for sperm production. Impaired gonadal function (hypogonadism) may result from decreased production of LH or FSH. Males affected by this disorder typically present with a lack of a normal sperm count .(Santi et al ., 2020) . The process of sperm formation is directly stimulated by the hormone FSH when it binds to receptors in Sertoli cells. The hormone LH stimulates Leydig cells to secrete more testosterone, which in turn acts on Sertoli cells and the surrounding cells of the seminiferous tubules, indirectly stimulating the process of sperm formation. (Li et al., 2024)

The decline in these hormones is attributed to the toxicity of the CP drug. The fluctuation in steroid metabolism may be partially due to the inhibition of serum testosterone levels associated with the administration of CP. (Tian et al., 2018) . The decrease mediated by CP in serum testosterone levels may be due to reduced responsiveness of Leydig cells to gonadotropins and the stress associated with the activity of steroid side chain cleavage (Kata, 2013, Sriram et al ., 2024). Additionally, the results suggest that the hormonal disturbances caused by cisplatin are mediated by its effects on the hypothalamic-pituitary-gonadal axis (Khamis et al., 2023). In addition, the results suggest that cisplatin-induced hormonal disturbances are mediated by its effects on the hypothalamic-pituitary-gonadal axis (Khamis et al ., 2023). The decrease in testosterone levels associated with CP treatment was shown to be dependent on the inhibition of luteinizing hormone receptor numbers and cytochrome P-450 levels in rat testes (Maines et al., 1990, Hassen et al., 2021) reported a similar decrease in P-450 concentration in rat testes. With this decrease, plasma testosterone levels were also found to be low. While treatment with Vit C and treatment with Vit C and CP resulted in a moral elevation in the concentration of LH, FST and Testosterone hormones compared with the control group. The hypothalamic-pituitary-gonadal axis (HPG axis) is the major signaling pathway responsible for the regulation of reproductive hormones. Sexual and reproductive hormones play a key role in regulating the reproductive system and, consequently, fertility. Oxidative stress affects testosterone production, and reducing

oxidative stress improves hormone levels. Vit C is one of the powerful antioxidants that accounts for up to 65% of the antioxidant activity in semen. (Xie et al., 2022).
The GnRH hormone secreted by the hypothalamus stimulates the activity of the gonads. FSH primarily acts on the Sertoli cells of the testes to stimulate sperm formation and maintain the maturation of sperm cells, while LH acts on Leydig cells to enhance androgen production within the testes, the most prominent of which is testosterone, which is essential for sperm formation (Oduwole et al., 2021)

It was observed that the levels of FSH and LH in serum improved significantly with vitamin C supplementation, and that the pituitary gland is an important site for the absorption of vitamin C, which can enhance the levels of the two hormones after oxidative damage caused by CP intake. Additionally, vit C increases the concentration of glutathione and the activity of antioxidant enzymes such as catalase and superoxide dismutase, which are vital for the survival of sperm.(Olorunshola et al., 2011; Stöter et al., 2013).Vit C is a vitamin transporter that activates the secretion of both FSH and LH from the pituitary gland, assuming that vit C is stocked in secretory granules that also contain LH and FSH and is released with the two hormones by exocytosis (Kothari et al., 2017). Once it leaves the cell membrane,It is transmitted by Vit C carrier to the cells. When it enters the cell, It stimulates an increase in intracellular Ca2+In turn, it binds to calmodulin and activates NOS, which in turn releases NO. NO stimulates cAMP production from Gs-binding guanylate cyclase in the pituitary gland. It is therefore possible that vitamin C stimulates the release of LH-RH and FSH-RH with the resulting secretion of gonadotropins FSH and LH by NO. (Okon and Utuk, 2016)

The improvement in testosterone concentration observed in the vitamin C and CP group may indicate that vitamin C helps to alleviate cisplatin-induced testicular changes and because vit C has antioxidant properties that have been shown to protect tissues from reactive oxygen species, since vit C affects the hypothalamic-pituitary-testicular axis, raising serum testosterone levels (Ashamu et al., 2010). Vit C deficiency causes oxidative stress in the testes, which interferes with testosterone production and spermatogenesis (Rekha et al., 2009). Vit C is a potent antioxidant with high concentrations within the testis, capable of restoring oxidative balance in the testicular environment and cellular oxidation of Leydig cells,This interpret our results which indicated that vit C associated with lifting androgenic status in susceptible males to oxidative stress (Colagar, and Marzony, 2009). We also note that treatment with the alcoholic extract of Silybum marianum and treatment with the alcoholic extract of Silybum marianum and CP together led to an increase in the concentration of the hormones LH, FST and testosterone compared to the healthy group.Silybum marianum extract is used in the treatment of many physiological disorders (Surai PF, 2015). It is a flavonoid and polyphenolic molecule, extracted from the seeds of the plant (Soleimani. et al. 2019). Silybum marianum contains many active compounds, the most important of which is silymarin, which is effective in many conditions including infertility, these compounds act as antioxidants (Zarif-Yeganeh and Rastegarpanah, 2019). Several studies have demonstrated the protective and antioxidant properties of silymarin against the side effects of chemotherapy drugs and environmental toxins on sperm (Aghashahi et al., 2020). Silybum marianum treatment is effective in improving sperm parameters and fertility against all toxins. (Choobineh et al., 2018).Research has shown that silymarin increases the concentration of norepinephrine, a factor that may affect the hypothalamic-pituitary-testicular axis, and increases the secretion of LH and FSH through the synthesis of nitric oxide.(Hamid et al., 2018).There is a relationship between LH concentration and sperm count, LH increases testosterone secretion by binding to the Leydig cell. Testosterone is an important factor in spermatogenesis (Abedi et al., 2016). By binding to Sertoli cells, FSH can increase the concentration of ABP (androgen binding protein) and ABP can increase the concentration of testosterone in the seminiferous tubules to promote spermatogenesis (Oufi et al., 2012).On the other hand, silymarin can show its antioxidant properties in five ways, such as directly scavenging free radicals,

prevents the formation of free radicals by inhibiting the enzymes responsible for their production or by maintaining the electron transport chain in the mitochondria, where it maintains optimal redox conditions for the cell through the activation of a group of antioxidant enzymes and non-enzymatic antioxidants, activate genes responsible for the synthesis of protective molecules, including HSP (heat shock proteins) and thioredoxin, and reduce inflammatory responses by inhibiting NF-κB (nuclear factor-κB) pathways.(He et al., 2017, Kamali et al., 2020).

Through tissue observation in the picture(B1, B2) , we found that animals dosed with CP show the presence of a colloidal substance inside the tubules, incomplete sperm maturation, destruction of the seminiferous tubules, destruction of Leydig cells, and sperm necrosis. demonstrating its toxicity to all types of germ cells and spermatogenesis (Zhu et al., 2024). Cytotoxic drugs are known to inhibit spermatogenesis by causing the death of developing germ cells in the seminiferous tubules. This leads to the elimination of active sperm cells and thus leads to decreased daily sperm production (Garcia, 2021). Germ cells, especially differentiated sperm cells, are highly susceptible to toxic agents due to their rapid proliferation (Marcon, 2011). Low testosterone levels in the current study due to the drug effect may be responsible for the decreased sperm number and formation in CP-injected rats (Rahimi et al., 2022, Wang et al .,2020). Low testosterone levels lead to germ cell depletion at complex stages of the seminiferous epithelium cycle of spermatogenesis (Park et al., 2020). Cisplatin-induced male reproductive toxicity may be increased by decreased serum luteinizing hormone and testosterone levels, as well as Sertoli cell damage, in addition to the direct toxic effect on germ cells (Filobbos et al., 2020).In addition, CP causes oxidative stress, which includes increased lipid peroxidation, disruption of the redox balance in tissues, and a decrease in the antioxidant system, as well as histological changes in testicular tissues. This result is due to oxidative stress. It is clear that oxidative stress and reactive oxygen species play an important role in the development of cisplatin toxicity (Aly & Eid.,2020, Corpuz-Hilsabeck and Kolte, 2023).Cisplatin-induced male reproductive toxicity may be increased by decreased serum levels of luteinizing hormone and testosterone, as well as damage to Sertoli cells, in addition to the direct toxic effect on germ cells (Filopos et al., 2020 , Keshta et al ., 2023)

CP also causes Leydig cell destruction and production of reactive oxygen species, and apoptosis has been found to play an important role in controlling sperm accumulation.(Rauf et al ., 2021).Hormone deficiency and exposure to chemotherapy drugs may lead to an increase in the frequency of programmed germ cell death (Ijaz et al., 2022), after a single dose of CP causes programmed death in the testes, Sertoli cells, germ cells and in the epididymis spermatozoa, testicular damage and seminiferous tubule destruction are induced (Rauf et al., 2021)

The results are shown in picture (D1, D2, F1, F2) part of the testes of the group treated with Silybum marianum extract and treated with Silybum marianum and CP together shows the seminiferous tubules in their normal form. The stages of sperm formation can also be observed with the observation of Leydig cells. One of the most important active compounds in Silybum marianum is silymarin which is considered one of the most important antioxidants (Javeed et al., 2022). It acts as a scavenger and removes free radicals, thus protecting sperm from oxidative damage. There is usually a balance between the concentration of reactive oxygen species (ROS) and the antioxidant oxidation reaction in the male reproductive system. (Agrawal et al., 2020). Polyunsaturated fatty acids and phospholipids are the major components of the sperm membrane and are highly susceptible to oxidation , the production of large amounts of ROS by immature sperm can overwhelm the antioxidant defense mechanisms of sperm and seminal fluid (Fatehi et al., 2018 , Abou-Elghait et al ., 2022).Since Silybum marianum prevents and removes free radicals, it protects sperm from oxidation. (Keshta et al., 2023). According to various studies conducted on humans and animals, silymarin, as a natural antioxidant, has

antioxidant and chemopreventive effects as well as tissue regenerative properties (Abou El-Gheit et al., 2022)

Silymarin can be used as a dietary supplement due to its chemical and radioprotective properties to protect sperm cells from harmful chemical and physical factors (Latacela et al., 2023). Moreover, reports indicate that silymarin as a radioprotective agent can reduce and even improve the harmful effects of radiation. Silymarin has also been shown to be a protective agent for sperm against sodium arsenite toxicity, and it is able to improve several sperm parameters such as motility, viability, and mitochondrial membrane potential of sperm (Bourhaydar et al., 2021). As a natural polyphenolic compound, silymarin can react with reactive oxygen species and free radicals and convert them into less toxic compounds and also enhances the effect of antioxidant enzymes such as glutathione and superoxide dismutase (Lamia et al., 2021)

As shown in the results in the picture (C1, C2, E1, E2), testicular tissue. Animals given vitamin C and treated with CP and Vit C shows the seminiferous tubules in their normal shape, and the stages of sperm formation can be observed with the observation of Leydig cells. Vit C is one of the well-known natural antioxidants, It is a water-soluble micronutrient necessary for biological functions and is associated with semen quality and fertility in humans. (Zhou et al., 2022)

Combined treatment with CP and vitamin C can prevent the harmful effects of CP and compensate for the decrease in mean sperm count, Leydig cells, sperm motility, and serum testosterone levels, and can reduce mean serum and tissue malondialdehyde levels (Sadeghzadeh et al., 2019)

Vitamin C can increase the concentration of glutathione (GSH) and the activity of antioxidant enzymes in the testis such as catalase and superoxide dismutase, which are essential for sperm survival by reducing oxidative stress-induced injuries (Raeeszadeh et al., 2021). On the other hand, vitamin C can increase the activity of 3b-HSD and 17b-HSD enzymes in the testis, which increases the production of male hormone and thus the number of sperm cells and superoxide dismutase(Amor., 2021). Vitamin C is also an important cofactor for the hydroxylation of collagens that causes interactions between testicular cells, which plays a major role in spermatogenesis, improving the differentiation of these cells, and finally increasing the number of cells and DSP (Swelum et al., 2022).

5. Conclusion

The article concludes that the cisplatin (CP)-induced damage to the male reproductive system, including reduced levels of LH, FSH, and testosterone, as well as histological damage to testicular tissue, is effectively mitigated by treatments with Silybum marianum seed extract and vitamin C. Both treatments demonstrated significant improvements in hormonal levels and restored normal testicular architecture and spermatogenesis. These findings highlight the antioxidant and protective roles of Silybum marianum and vitamin C, making them promising adjunct therapies to reduce the adverse effects of cisplatin on male reproductive health. Future research should explore the clinical implications of these findings and their potential applications in mitigating chemotherapy-induced reproductive toxicity.

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