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Physiology, Biochemistry, and Pharmacology Department

# Evaluation of Anti-oxidant Effects of Ginseng Extract Nanoparticles in Male Rats Exposed to Potassium Dichromate

## A Thesis

Submitted to the Council of the College of Veterinary Medicine, University of Kerbala in Partial Fulfillment of the Requirements for the Master Degree of Science in Veterinary Medicine / Physiology

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بسمِ اللهِ الرحمنِ الرحيمِ

﴿ وَيَسْأَلُونَكَ عَنِ الرُّوحِ قُلِ الرُّوحُ مِنْ أَمْرِ
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We certify that thesis entitled **(Evaluation of Anti-oxidant Effects of Ginseng Extract Nanoparticles in Male Rats Exposed to Potassium Dichromate)** has been prepared by **Mohammed Abd Ali Hamza** under my supervision at the college of Veterinary Medicine, University of Kerbala in partial fulfillment of the requirements for the Master of Degree in the Sciences of Veterinary Medicine in Physiology, Biochemistry and Pharmacology.

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## *Declaration*

I hereby declare that this dissertation is my original work except for equations and citations which have been fully acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at University of Kerbala or other institutions.

***Mohammed Abd Ali Hamza***

**/ / 2024**

## *Dedication*

**To the Messenger of Mercy, the Prophet Muhammad, "Allah may peace be upon him and his progeny..."**

**To my homeland, Iraq, which is bleeding with martyrs.**

**To my father, may God have mercy on him**

**And my beloved mother, who encouraged me to be faithful**

**For my dreams and aspirations..**

**To my wife for her great patience**

**My dream has come true and my beloved son...**

**To my brothers and sisters for their encouragement and love.**

**To everyone who benefits from this work...**

***Mohammed Abd Ali Hamza***

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## Summary

Potassium dichromate is a chemical compound containing chromate and potassium, it is a toxic substance used in various industries as a harmful chemical compound. Exposure to potassium dichromate can be hazardous to the environment and human health, Potassium dichromate has been shown to have detrimental effects on the reproductive system, exposure to this compound can lead to testicular damage and decreased sperm production in males. Nanotechnology refers to the use of materials and structures at the nanometer scale (one billionth of a meter). This technology allows the study and control of matter at the atomic and molecular level, opening up huge possibilities in a wide range of fields. In the medical field, nanotechnology can be used to develop and deliver drugs precisely to targeted areas in the body, increasing treatment effectiveness and reducing side effects. It can also be used to develop precise and efficient medical devices. This study explored the detrimental effects of potassium dichromate on the male reproductive system of rats and the potential protective role of ginseng in mitigating these effects. Forty-two adult male albino rats were divided into seven groups: Negative control group: Received normal saline daily for 4 weeks. Potassium dichromate group: Received 2 mg/kg body weight of potassium dichromate daily by intraperitoneal injection for 2 weeks. Positive ginseng group: Received ginseng orally at a dose of 200 mg/kg body weight daily for 4 weeks. Nano- ginseng group: Received nano-ginseng orally at a dose of 200 mg/kg body weight daily for 4 weeks. Potassium dichromate + ginseng group: Received potassium dichromate 2 mg/kg + ginseng orally at a dose of 200 mg/kg body weight daily for 4 weeks. Potassium dichromate + nano-ginseng (200mg/kg) group: Received potassium dichromate + nano-ginseng at a dose of 200 mg/kg body weight daily for 4 weeks. Potassium dichromate + nano-ginseng (100mg/kg) group: Received potassium

dichromate + nano-ginseng at a dose of 100 mg/kg body weight daily for 4 weeks. Blood samples were analyzed to measure luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, malondialdehyde (MDA), catalase (CAT), and superoxide dismutase (SOD) levels. Testicular and epididymal tissues were examined histologically. the result shaw  Exposure to potassium dichromate resulted in a significant decrease in testosterone, LH and FSH levels, indicating impaired testicular function. Oxidative stress was also induced, as evidenced by increased MDA levels and decreased CAT and SOD activities. These alterations were accompanied by histological changes in the testes and epididymis. Treatment with ginseng or nano ginseng ameliorated the adverse effects of potassium dichromate on the male reproductive system. Both ginseng forms restored hormone levels, reduced oxidative stress markers, and improved testicular and epididymal histology. The findings suggest the potential use of ginseng as a protective agent against potassium dichromate-induced reproductive toxicity in rats.

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# List of Abbreviations

| Abbreviations | Meaning |
|---|---|
| **4-HNE** | 4 hydroxynonenal . |
| **ANOVA** | Analysis of variance. |
| **CAT** | Catalase. |
| **DHT** | Dihydrotestesterone |
| **ELISA** | Enzyme-linked immunosorbent assay |
| **EWRTD** | Environment and water research and technology director . |
| **FSH** | Follicular Stimulating Hormone . |
| **FTIR** | Fourier-transform infrared. |
| **H2O2** | Hydrogen peroxide |
| **HPA** | hypothalamic-pituitary-adrenal |
| **HSD** | Honestly Significant Difference . |
| **IPA** | Institute for Public Accuracy. |
| **KCl** | Potassium Chloride |
| **Kg** | Kilogram |
| **LH** | Luteinizing Hormone . |
| **MDA** | Malondialdehyde . |
| **Mg** | Milligram |
| **Mg/dl** | Milligrams per deciliter |
| **Mg/kg** | Milligram per kilogram |
| **NBT** | Nitroblue tetrazolium. |
| **NPs** | Nanoparticles |
| **$O2^-$** | superoxide anion |
| **P** | Probability values . |

| | |
|---|---|
| **PDC** | Potassium di chromate . |
| **PPE** | Personal protective equipment |
| **ROS** | Reactive oxygen species |
| **SEM** | The scanning electron microscope . |
| **Se-NPs** | Selenium nanoparticles |
| **SOD** | Superoxide Dismutase. |
| **TBA** | Thiobarbituric Acid . |
| **TCDD** | 2,3,7,8-Tetrachlorodibenzo-p-dioxin. |
| **TCM** | Traditional Chinese Medicine . |
| **Uv-vis** | Ultraviolet–visible |
| **XOD** | Xanthine oxidase. |
| **XRD** | X-ray diffraction . |
| **MAPK** | mitogen-activated protein kinase |
| **NF-kB** | nuclear factor kappa B |
| **Cr(VI)** | hexavalent chromium |
| **Cr(III)** | trivalent chromium |
| | |

# Chapter One
# Introduction

# Introduction

The compound potassium dichromate is a chemical compound containing chromate and potassium. It is a toxic substance used in various industries as a harmful chemical compound. Exposure to potassium dichromate can be hazardous to the environment and human health, causing poisoning and damage to the respiratory, digestive, and nervous systems. Its toxicity is attributed to its ability to impact cellular vitality ( **Goullé *et al.*,2012** ).

Potassium dichromate has been shown to have detrimental effects on the reproductive system. Exposure to this compound can lead to testicular damage and decreased sperm production in males. Additionally, it can also affect the female reproductive system by causing damage to the ovaries and reducing fertility ( **Bashandy *et al*.,2021**).

Furthermore, potassium dichromate has been linked to an increased risk of developing certain types of cancer, including lung cancer and nasal cavity cancer, which can further impact reproductive health. It's essential to handle this compound with extreme caution and adhere to safety guidelines to minimize the risk of exposure and its potential impact on the reproductive system ( **Rasool *et al*.,2014**)

Nanotechnology refers to the use of materials and structures at the nanometer scale (one billionth of a meter). This technology allows the study and control of matter at the atomic and molecular level, opening up huge possibilities in a wide range of fields (**Sahu *et al*., 2023**).

The benefits of nanotechnology include the development of new materials with unique properties such as strength, flexibility, and thermal conductivity, as well as high-precision, low-cost manufacturing. Nanotechnology can be applied in areas such as medicine, electronics, energy, the environment, materials science, and many other applications ( **Bayda *et al*.,2019**).

In the medical field, nanotechnology can be used to develop and deliver drugs precisely to targeted areas in the body, increasing treatment effectiveness and reducing side effects. It can also be used to develop precise and efficient medical devices ( **Barhoum *et al*.,2022**).

Nanoparticles are particles with dimensions on the nanoscale, typically ranging from 1 to 100 nanometers. The creation of nanoparticles, or nanosynthesis, is a crucial aspect of nanotechnology, and it holds significant importance across various scientific and technological fields (**Jha *et al*.,2014**).

One common method for synthesizing nanoparticles is through bottom-up or top-down approaches. Bottom-up methods involve the assembly of small building blocks into larger structures, while top-down methods involve breaking down larger structures into smaller components. These methods enable the precise control of size, shape, and composition, allowing scientists to tailor nanoparticles for specific applications (**Swati Kumari *et al*.,2023**).

The importance of nanoparticle synthesis stems from the unique properties exhibited by materials at the nanoscale. These properties can differ significantly from those at larger scales, leading to novel and enhanced characteristics. Some key aspects include : Size-Dependent Properties nanoparticles exhibit size-dependent properties, such as altered chemical reactivity, increased surface area, and quantum effects. These unique characteristics can be exploited in various applications ( **Li *et al*.,2019**).

Biomedical Applications in medicine, nanoparticles are utilized for drug delivery, imaging, and diagnostics. The small size allows for targeted delivery to specific cells or tissues, minimizing side effects and improving treatment efficacy. Catalysis nanoparticles serve as efficient catalysts due to their increased surface area, which enhances catalytic activity. This has implications

for various industrial processes, including environmental remediation and energy production (**Barhoum *et al*.,2022**).

Electronics and Photonics nanoparticles play a crucial role in the development of advanced electronics and photonics devices. They can be incorporated into materials to enhance conductivity, optical properties, and overall device performance, Energy Storage and Conversion nanoparticles are employed in the development of energy storage devices, such as batteries and supercapacitors, as well as in energy conversion technologies like solar cells. Their unique properties can improve the efficiency and performance of these devices ( **Tarafdar *et al*.,2013**).

Materials Science nanoparticles contribute to the creation of advanced materials with improved mechanical, thermal, and electrical properties. This has implications for industries ranging from construction to aerospace, environmental application nanoparticles can be utilized for environmental monitoring and remediation (**Dabirian *et al*.,2023**).

Ginseng is a popular herbal remedy that has been used in traditional medicine for centuries, particularly in East Asia. The term "ginseng" typically refers to the roots of plants in the Panax genus, including Panax ginseng (Asian or Korean ginseng), Panax quinquefolius (American ginseng), and Panax notoginseng (Chinese ginseng). Ginseng is often classified as an adaptogen, which means it may help the body adapt to stress and restore balance. It is believed to have a normalizing effect on bodily functions (**Maria *et al*.,2023**).

In traditional medicine, ginseng has been used to boost energy, improve cognitive function, enhance stamina, and support the immune system. It is also believed to have anti-inflammatory and antioxidant properties (**Fuxun Yang, *et al*.,2023**).

Ginsenosides are the primary active compounds in ginseng. These compounds are believed to contribute to the herb's pharmacological effects. The composition and concentration of ginsenosides can vary between different types of ginseng (**Ratan *et al*.,2021**).

Research on ginseng's health benefits is ongoing, and some studies suggest potential positive effects on cognitive function, immune system support, and energy metabolism. However, more research is needed to establish definitive conclusions ( **Kim J. H., 2018**) (**Maria *et al*.,2023**).

**Aims of the Study:**

The present study was undertaken to prepare and fabricate nano Ginseng, loaded on selenium nanoparticles, We study the efficacy of nanoparticle of ginseng as an antioxidant against Potassium dichromate toxicity on fertility and physiological, hormonal value and histopathological examination in male rats.
The aim of study is performed via the following objectives:

1. Characterization of nanomaterial by (UV, FTIR.SEM, and XRD).
2. Measuring the level of (CAT, SOD, and MDA).
3. Hormones (LH, FSH and Testosterone).
4. Histopathological examination of the testis and epididymis.

# Chapter Two
# Literature Review

# 2. Literature Review

## 2.1 Nanotechnology and nanoparticles :

Nanotechnology is the science that deals with the matter at the size 1 billionth of a matter ( $10^{-9}$ m= 1 nm ) and also could be defined as the study of manipulating matter at the molecular and atomic scale . The typical size is ranged between 1 nanometer to 1 micrometer (**Bhushan 2017**) . Nanotechnology field is the modern science of material and is the most active fields . Nanoparticles show specific properties and improved characteristics such as distribution , size , and morphology . The Nano material's and nanoparticles have new application which are progressing rapidly ( **Naiwa, 2000 ; Murphy,2008 and Mohanta, 2017** ).

Nanos, a Greek term denoting extreme minuteness, serves as the origin of the word "nano." Various types of nanoparticles, such as carbon, polymeric, metal, ceramic, semiconductor, and lipid nanoparticles, can be categorized based on their morphology and physical/chemical attributes (**Varghese *et al.*, 2019**). Among these, polymeric nanoparticles have garnered significant attention due to their distinct advantages over other nanoparticle types and their pioneering contributions to both polymer science and nanotechnology (**Zhang *et al*., 2008**). Polymeric nanoparticles offer numerous benefits, including streamlined preparation processes, precise control over particle size distribution, and effective drug retention and protection (**Sur *et al*., 2019**).

The demand for modified and targeted drug delivery systems is escalating, primarily because of their ability to facilitate controlled drug release, site-specific action, and enhanced patient compliance (**Kaushik *et al*., 2014**). Polymers play a pivotal role as the foundational framework for developing such delivery systems, with biocompatible polymers experiencing remarkable growth and thus dominating discussions in the field (**Lee *et al*., 2020**).

Nanoparticles, functioning as colloidal particles, are employed to achieve targeted drug delivery within the body (**Xiao *et al.*, 2022**).

Due to huge application of nanomaterial in the field of physics , chemistry , biology , and medicine there are many research made on synthesized Nano materials and their characterization is an emerging field of Nano technology from the past years (**Song and Kim 2008**) .

They can be synthesized by using many methods including chemical and physical (**Iravani *et al .*, 2014**) , electrochemical (**Lapp *et al.*, 2018** ) thermal method (**Goudarzi *et al.*, 2016**) and Photochemical (**Pu *et al.*, 2018**) .

Recently the green method for synthesis of Nano particles have been emerged due to ecofriendly economic method . In this method the plant extract is used reducing and stabilizing agent . A number of plant extracts is used in the synthesis of selenium nanoparticles (SNPs) such as Elephantopus scaber (**Francis *et al.*, 2018** ) , and Thymbra spicata (**Veisi *et al.*, 2018**) .

### 2.1.1 Selenium nanoparticles.

Selenium nanoparticles stand at the intersection of nanotechnology and biomedicine, offering a wealth of applications that extend beyond their elemental origins. Selenium, recognized for its essential role in human health, takes on new dimensions when engineered into nanoparticle form, creating a versatile and promising field of study (**Zhang *et al.*,2023**).

In the realm of biomedical applications, selenium nanoparticles exhibit remarkable antioxidant properties, acting as potent defenders against oxidative stress and cellular damage as shown in Fig.(2.1).Their potential anti-cancer effects are under scrutiny, showing promise in inhibiting the growth of cancer cells. Beyond this, the unique attributes of selenium nanoparticles find

application in drug delivery systems, where their biocompatibility makes them ideal carriers for targeted therapeutic interventions (**Ananth *et al.*,2019**).

Moving into the arena of antimicrobial activity, selenium nanoparticles reveal antibacterial prowess, suggesting applications in combating microbial infections. Their antifungal effects broaden their utility, providing potential solutions for addressing fungal infections that pose significant challenges in healthcare (**Djanaguiraman *et al*.,2018**).

In materials science, selenium nanoparticles bring catalytic properties to the forefront, contributing to catalysis in various industrial processes. Their unique optical and electronic properties position them as key players in the development of optoelectronic devices, hinting at advancements in technology (**Nayak *et al*.,2021**).

Environmental remediation benefits from the capabilities of selenium nanoparticles, particularly in heavy metal removal from water. These nanoparticles show promise in pollution control strategies, aligning with the growing need for sustainable environmental practices (**Shahabadi *et al*.,2021**).

However, the exploration of selenium nanoparticles is not without its challenges. The potential toxicity, especially in elevated concentrations, demands careful consideration. Standardization of synthesis methods and characterization techniques are crucial to ensuring reproducibility and safety in applications (**Khurana *et al*.,2019**).

selenium nanoparticles emerge as versatile entities with profound implications for human health, materials science, and environmental sustainability. Ongoing research endeavors seek to harness their benefits while navigating the complexities and challenges to usher in responsible and effective applications in various domains (**Zhang *et al*.,2023**).

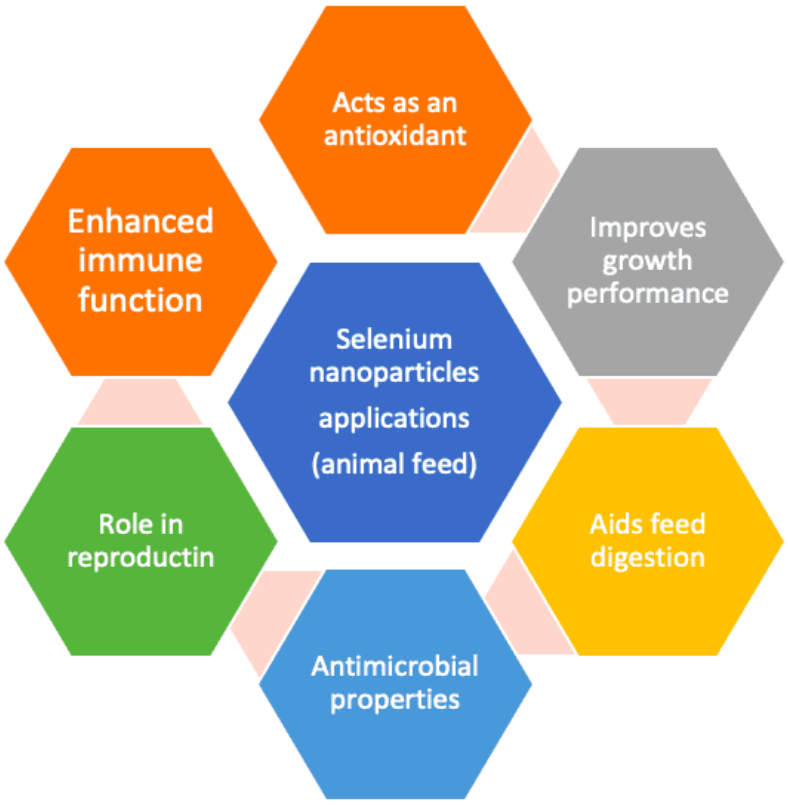



**Figure (2.1) Applications of SeNPs in animal feed applications. (Abadi *et al*.,2023)**

## 2.1.2 Pharmacokinetics of selenium nanoparticales.

The pharmacokinetics of selenium nanoparticles is a comprehensive exploration into the intricate processes governing their behavior within the human body. This field of study unravels the dynamics of absorption, distribution, metabolism, and excretion, shedding light on bioavailability, interactions, and potential therapeutic applications (**Ullah *et al*.,2022**).

In terms of absorption, selenium nanoparticles can enter the body through ingestion, inhalation, or skin contact. The mechanisms of absorption are influenced by particle size, surface characteristics, and the physiological environment (**Hosnedlova *et al*.,2018**).

Once absorbed, these nanoparticles enter the bloodstream and disperse throughout the body. Distribution is affected by factors like blood flow, tissue

perfusion, and the specific physicochemical properties of the nanoparticles ((**Zhang *et al.*,2021**).

Metabolically, in the liver, selenium nanoparticles may undergo transformations, including the reduction of selenium species. Enzymatic processes play a role in these transformations, influencing bioavailability and toxicity (**Shar *et al*.,2019**).

Elimination pathways involve renal excretion through urine, fecal excretion, or clearance through the hepatobiliary system. The rate of excretion depends on particle characteristics such as size, surface charge, and overall biocompatibility (**Gunti *et al*.,2019**).

Factors influencing pharmacokinetics include particle characteristics, chemical form, and individual physiological variations. Tailoring nanoparticle properties can enhance targeted delivery, optimizing therapeutic outcomes (**Pyrzynska & Sentkowska, 2022**).

Understanding the pharmacokinetics of selenium nanoparticles is crucial for their therapeutic efficacy. It provides insights into the complexities, allowing for the refinement of methodologies and a more comprehensive understanding (**Ahamed *et al*.,2022**).

In general, the pharmacokinetics of selenium nanoparticles serves as a roadmap for researchers and clinicians, guiding the design of nanoparticles for therapeutic purposes. This understanding is essential for maximizing benefits while minimizing potential adverse effects, fostering innovative applications in medicine and beyond (**Gunti *et al*.,2019**).

## 2.1.3 Medical application of selenium nanoparticles.

In the expansive landscape of medical science, selenium nanoparticles have emerged as promising agents, leveraging their unique properties to offer diverse applications with potential therapeutic benefits (**Geoffrion *et al*.,2020**).

Selenium nanoparticles exhibit robust antioxidant properties, a key attribute in combating oxidative stress implicated in various health conditions, including neurodegenerative diseases and cardiovascular disorders (**Mellinas *et al*.,2019**).

Beyond antioxidant capabilities, research indicates the anti-cancer potential of selenium nanoparticles. Their demonstrated inhibitory effects on cancer cell growth open avenues for potential applications in cancer therapy (**Puri *et al.,* 2024**).

Biocompatibility is a notable feature, rendering selenium nanoparticles suitable carriers for drug delivery systems. Their tailored properties enable precise and targeted delivery of therapeutic agents to specific cells or tissues, enhancing treatment efficacy. The nanoparticles also reveal antibacterial and antifungal properties, suggesting potential applications in addressing microbial infections and offering new possibilities for developing antimicrobial therapies (**Liu *et al*.,2018**)

In the realm of diagnostics, selenium nanoparticles serve as contrast agents in imaging techniques, enhancing the visibility and accuracy of diagnostic procedures. This application is particularly valuable in medical imaging technologies (**Jang *et al.,* 2011**).

Selenium nanoparticles hold promise in neuroprotection due to their antioxidant capabilities. They may contribute to mitigating oxidative stress-

related damage in the nervous system, presenting potential therapeutic interventions for neurological disorders (**Zhang *et al*.,2020**).

In the field of wound healing, selenium nanoparticles exhibit properties conducive to the process. Their application in wound dressings or topical formulations has the potential to enhance healing and reduce inflammation (**Ahamed *et al*.,2022**).

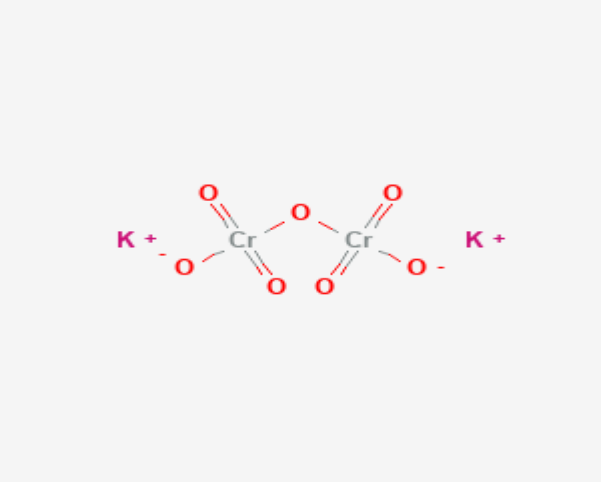
Immunomodulation is another avenue of exploration, as selenium nanoparticles have been studied for their effects on the immune system. Their influence on immune responses holds potential for contributing to overall health (**Chen *et al*.,2022**).

selenium nanoparticles represent a multifaceted approach to addressing various health challenges, from antioxidant capabilities to anti-cancer potential and targeted drug delivery. Their applications open new frontiers in medical research and therapeutics, potentially revolutionizing healthcare solutions (**Kieliszek *et al.*,2022**).

## 2.2 Potassium dichromate:

potassium dichromate is a chemical compound containing the elements potassium and chromium, represented by the chemical formula K2Cr2O7. Potassium dichromate is a strong orange-colored substance and has applications in industries and chemistry(**National Center for Biotechnology Information ,2024**).

In the context of the research mentioned in the previous inquiry, potassium dichromate is used as a pollutant or toxin to which male rats are exposed. This is done to study its effects on physiological parameters and fertility(**Monga *et al*., 2022**) **(Hartwig *et al.*,2016).**




Fig(2.2) potassium dichromate structure(Monga *et al*., 2022)

## 2.2.1 History of potassium dichromate.

Potassium dichromate, with the chemical formula K2Cr2O7, has a notable history in the realm of chemistry. It was first discovered by the French chemist Louis Nicolas Vauquelin in 1797, Vauquelin isolated this compound by mixing a solution of potassium carbonate with a lead chromate mineral called crocoite. The resulting bright orange crystals were identified as potassium dichromate (**Hammond,2000**).

The compound gained prominence due to its distinctive color and unique chemical properties. Potassium dichromate became widely used in various applications, including as a strong oxidizing agent in chemical laboratories. Its ability to readily provide hexavalent chromium ions makes it valuable in oxidation-reduction reactions (**Raghunathan *et al*.,2009**).

Over the years, potassium dichromate has found applications in industries such as photography, where it was used in color development processes. It has also been employed in textile dyeing and as a corrosion inhibitor. However, its use has declined in some areas due to environmental and health concerns associated with hexavalent chromium compounds, which are considered toxic and carcinogenic (**Jacobs *et al*.,2016**).

The compound's history reflects its significance in chemical processes and various industrial applications, while contemporary considerations focus on balancing its utility with potential environmental and health risks (**Monga *et al*., 2022**).

## 2.2.2. Chemical and physical properties of potassium dichromate.

Potassium dichromate (K2Cr2O7) is a powerful oxidizing agent. It readily donates oxygen atoms and can facilitate oxidation reactions. In solution, potassium dichromate dissociates to produce hexavalent chromium ions (Cr(VI)). These ions play a crucial role in various redox reactions. Potassium dichromate is acidic in nature. In aqueous solutions, it can react with water to produce chromic acid and potassium hydroxide. The compound exhibits a distinct color change during chemical reactions. For example, it changes from orange to green when reduced to chromium(III) ions ,while the physical properties of potassium dichromate is a bright orange-red crystalline solid, imparting a vivid color to its appearance.It is highly soluble in water ( (**Merja *et al*.,2018**).

The solubility increases with higher temperatures.The compound has a relatively high melting point, around 398 °C (748 °F).Potassium dichromate has a density of approximately 2.676 g/cm³.The crystals typically have an orthorhombic crystal structure.The molar mass of potassium dichromate is about 294.19 g/mol (**Hartwig *et al*.,2016**).

Understanding these properties is essential for manipulating potassium dichromate in various chemical processes and applications, including its use as an oxidizing agent in laboratories and industries. Additionally, awareness of its chemical and physical characteristics is crucial for handling it safely, considering its potential toxicity (**Gerd Anger *et al*.,2005**).

**Figure (2.3) Potassium dichromate (Gerd Anger *et al.*,2005)**

## 2.2.3 Production and uses of Potassium dichromate :

### 2.2.3.1 Production .

Potassium dichromate (K2Cr2O7) is typically produced through the reaction between sodium dichromate and potassium chloride. The process involves the following steps (**Merja *et al*.,2018**).

a.Formation of Sodium Chromate: Sodium dichromate (Na2Cr2O7) is initially produced by oxidizing chromite ore (FeCr2O4) with sodium carbonate in the presence of air **( Escudero Castejon, L.2018).**

$$FeCr2O4+8Na2CO3+7O2\rightarrow 8Na2CrO4+2Fe2O3+8CO2$$

b. Conversion to Potassium Dichromate: Sodium chromate is then reacted with potassium chloride (KCl) to yield potassium dichromate and sodium chloride **Sui, J. (2019).**

$$2Na2CrO4+2KCl\rightarrow K2Cr2O7+2NaCl$$

c.Crystallization: The resulting potassium dichromate is obtained by crystallization from the solution (**Gerd Anger *et al*.,2005**).

## 2.2.3.2. Uses .

a. Oxidizing agent: Potassium dichromate is a powerful oxidizing agent and finds extensive use in various oxidation-reduction reactions. It is commonly employed in laboratories for oxidizing organic compounds.

b. Colorant: In the past, potassium dichromate was widely used in the production of colored glass and ceramics due to its intense orange-red color.

c. Photography: It has been used in photography as a component of certain developing solutions.

d. Textile industry: Potassium dichromate has been used in the textile industry for dyeing fabrics.

e. Corrosion inhibitor: In some applications, it is used as a corrosion inhibitor for certain metals.

f. Analytical chemistry: It is used in analytical chemistry for determining the concentration of iron and as a titrating agent.

It's worth noting that the use of potassium dichromate has declined in some applications due to environmental and health concerns associated with hexavalent chromium, which is a known toxic and carcinogenic compound. Alternatives are sought where possible to mitigate these concerns (**Merja *et al*.,2018**).

## 2.2.4 Exposure to potassium dichromate.

Exposure to potassium dichromate, either through inhalation, ingestion, or skin contact, poses serious health risks due to the toxic nature of hexavalent chromium. Hexavalent chromium compounds, such as those found in potassium dichromate, are known to be carcinogenic and can cause various adverse health effects (**Ahamed *et al*.,2022**).

There are some potential routes of exposure and associated risks like Inhalation risks ,breathing in potassium dichromate dust or fumes can lead to respiratory irritation, lung damage, and an increased risk of lung cancer, Another ways for exposure are occupational settings,workers in industries where potassium dichromate is used, such as in metalworking, electroplating, or the production of certain chemicals, may be at risk of inhalation exposure. Also ingestion risks of swallowing potassium dichromate can cause severe damage to the gastrointestinal tract (**Al-Mukhtar *et al*.,2016**).

Chronic exposure through ingestion may lead to systemic toxicity, affecting internal organs. Accidental ingestion can occur in occupational settings or through contaminated water or food sources. Direct skin contact with potassium dichromate can result in irritation, burns, and allergic reactions. Prolonged or repeated exposure may cause dermatitis (**Jacobs *et al*.,2016**).

Workers handling potassium dichromate without proper protective measures, such as gloves and protective clothing, are at risk. Chronic exposure to hexavalent chromium, including potassium dichromate, is associated with an increased risk of lung cancer, as well as other respiratory and skin conditions, Industries where potassium dichromate is used should implement strict safety measures to minimize long-term exposure risks (**Al-saadi,2017**).

## 2.2.4.1 Environmental impact risks.

Improper disposal or release of potassium dichromate into the environment can lead to soil and water contamination, impacting ecosystems and posing risks to aquatic life, Environmental agencies regulate the disposal and release of chromium compounds to minimize their environmental impact. Given the health risks associated with potassium dichromate, it is crucial to handle and use it with extreme caution (**Jacobs *et al*.,2016**).

Occupational safety measures, including the use of personal protective equipment (PPE), proper ventilation, and adherence to safety protocols, are essential to minimize the risk of exposure in industrial settings. In addition, regulatory guidelines and environmental controls are in place to mitigate the impact on public health and the environment **(Arivarasu *et al.*,2008**).

### 2.2.5 Toxokinetics of potassium dichromate :

Exposure to potassium dichromate can pose significant toxicity risks to both humans and animals due to the presence of hexavalent chromium, a highly toxic form of chromium. Hexavalent chromium compounds, including those found in potassium dichromate, are known to be harmful to various organs and systems within the body. The term toxicokinetics refers to the study of the absorption, distribution, metabolism, and elimination (ADME) of a substance in the body. In the case of potassium dichromate, understanding its toxicokinetics helps to comprehend how the body processes and responds to this toxic compound (**Bashandy *et al.*,2019**).

#### 2.2.5.1 Absorption .

When potassium dichromate is inhaled, it can be absorbed in the respiratory tract, primarily in the lungs. Fine particles or mists of potassium dichromate are more easily absorbed than larger particles, Potassium dichromate can be absorbed in the gastrointestinal tract after ingestion. The compound may dissolve in the stomach, releasing hexavalent chromium for absorption (**Jacobs *et al.*,2016**).

Absorption in the stomach and small intestine: absorption mainly occurs in the stomach and the upper part of the small intestine, also it can be absorbed by skin (**Tchounwou *et al.*,2012**).

## 2.2.5.2 Distribution and metabolism of potassium dichromate.

Following absorption into the bloodstream, potassium dichromate, a compound containing hexavalent chromium, undergoes distribution throughout the body. This distribution is facilitated by blood circulation and is influenced by factors such as solubility and the chemical form of chromium. Once in the bloodstream, potassium dichromate is transported to various tissues and organs. Notably, the compound tends to accumulate in specific areas, including the liver, kidneys, lungs, bone marrow, and other organs (**Kikuchi *et al.*,2017**).

Regarding metabolism, potassium dichromate undergoes a crucial process of reduction within the body. This reduction primarily occurs in the liver and involves the conversion of hexavalent chromium (Cr(VI)) to trivalent chromium (Cr(III)). Enzymatic processes, particularly those involving cellular reductases, play a key role in this conversion. The reduction of hexavalent chromium to trivalent chromium is considered a detoxification mechanism, aiming to mitigate the toxic effects associated with hexavalent chromium exposure (**AlAbdulaal *et al*.,2023**).

However, it's important to note that trivalent chromium, while generally less toxic than its hexavalent counterpart, can still have adverse health effects, especially with prolonged exposure. Throughout this metabolic process, reactive intermediates may be formed, potentially contributing to the overall toxic effects of chromium compounds (**Bhilkar *et al.*,2023**).

The distribution of potassium dichromate involves its transportation via the bloodstream to various organs, with a propensity for accumulation in specific tissues. Metabolism, primarily occurring in the liver, focuses on the reduction of hexavalent chromium to trivalent chromium as a detoxification mechanism. Understanding these processes is fundamental for assessing the

toxicological profile and potential health risks associated with exposure to potassium dichromate (**Emshary *et al*.,2021**).

## 2.2.5.3 Excretion and /or retention .

After distribution and metabolism within the body, the fate of potassium dichromate involves excretion and/or retention. Excretion is the process through which the body eliminates substances, while retention refers to the prolonged presence or accumulation of a compound in certain tissues or organs (**Tchounwou *et al*.,2012**).

Potassium dichromate, or more specifically, the resulting trivalent chromium after metabolic reduction, is primarily excreted from the body through urine. The kidneys play a crucial role in this elimination process, as they filter the bloodstream and excrete waste products, including chromium, into the urine. Urinary excretion is the main route through which the body rids itself of chromium, representing the final step in its elimination (**Ibrahima *et al*.,2018**).

However, it's essential to note that not all chromium is excreted immediately, and a portion may be retained in tissues. Chromium, especially trivalent chromium, can accumulate in specific organs, such as the liver and kidneys, leading to tissue retention. Prolonged exposure or chronic ingestion of potassium dichromate may result in increased levels of chromium in these organs (**Bhilkar *et al*.,2023**).

The balance between excretion and retention is dynamic and influenced by various factors, including exposure levels, duration, and individual physiological differences. The body's ability to eliminate chromium and the efficiency of the detoxification mechanisms contribute to the overall excretion and retention dynamics (**Bashandy *et al*.,2021**).

Understanding the excretion and retention of potassium dichromate is crucial for evaluating its potential long-term effects and assessing the risk of chronic exposure. Monitoring urinary chromium levels and studying tissue concentrations help researchers and healthcare professionals gain insights into the body's handling of this compound, informing risk assessments and safety guidelines (**Arivarasu *et al.*,2008**).

## 2.2.6 Effect of potassium dichromate on reproductive system.

Exposure to potassium dichromate, particularly due to its hexavalent chromium component, has been associated with significant impacts on the reproductive system, affecting both males and females (**Bashandy *et al.*,2019**).

In males, the adverse effects primarily manifest in disruptions to spermatogenesis, the process of sperm production. Studies have shown a decrease in sperm count and motility in response to potassium dichromate exposure. Additionally, the compound has been linked to testicular damage, including structural alterations and changes in seminiferous tubules. Oxidative stress induced by hexavalent chromium may further compromise sperm quality. Genotoxic effects have also been observed in testicular cells, raising concerns about genetic damage and mutations. Furthermore, there is evidence suggesting hormonal disruption, potentially affecting the balance of testosterone and other hormones crucial for male reproductive health (**Mary Momo *et al.*,2019)( Sharma *et al.*, 2020).**

For females, potassium dichromate exposure has been associated with ovotoxicity, impacting ovarian function and reducing fertility. Studies have indicated embryotoxic effects, posing risks to embryo development and potentially affecting pregnancy outcomes. Similar to males, females may experience hormonal imbalances, disrupting reproductive processes. Genotoxic effects in oocytes raise concerns about genetic damage within the female

reproductive system (**Bashandy *et al.*,2021**)( **Choudhuri *et al.*,2021**).Chromium treatment could severely affect the fertility potential of males through the promotion of OS as show in fig(2.4)( **Pereira *et al.*,2021**).

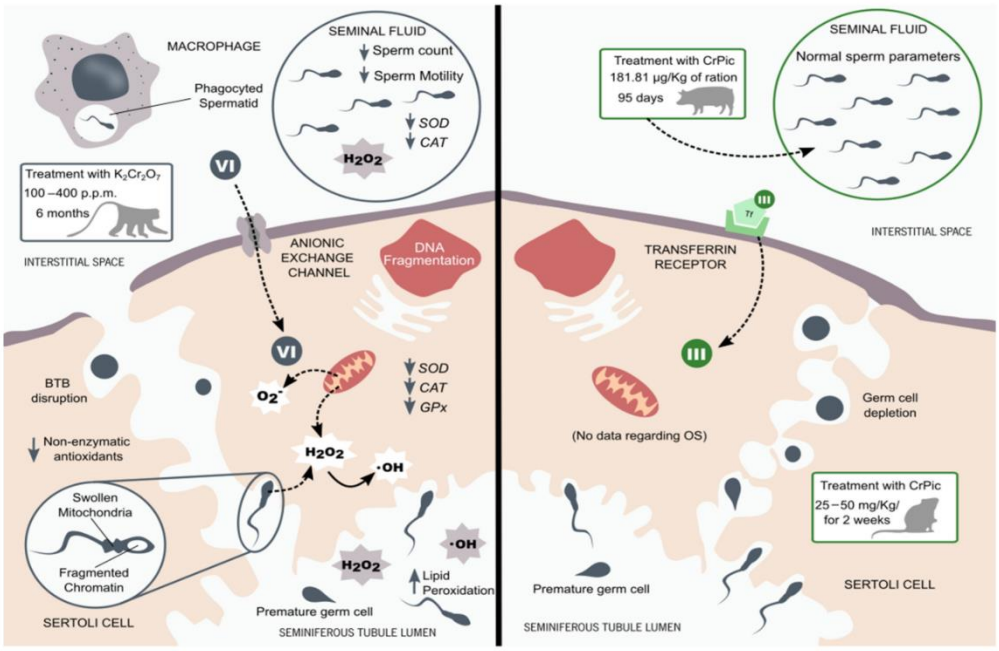



**Figure (2.4)Chromium effects in males' reproductive system (Pereira *et al.*,2021)**

It's important to recognize that the reproductive toxicity of potassium dichromate is often dose-dependent, with higher concentrations or prolonged exposure leading to more pronounced effects. Various routes of exposure, such as occupational settings or environmental contact, can contribute to reproductive health risks (**Hadi and Dohan,2018**).

In general potassium dichromate poses a threat to the male and female reproductive systems, potentially resulting in impaired fertility, developmental abnormalities, and other reproductive health issues. Mitigating exposure through safety measures and precautions is crucial to safeguarding reproductive health in both occupational and environmental contexts (**Bhilkar *et al.*,2023**).

## 2.2.7 Potassium Dichromate and Free Radical Generation in the Body.

Potassium dichromate, a chemical compound containing hexavalent chromium, is known to influence the generation of free radicals in the body. Free radicals are highly reactive molecules or atoms with unpaired electrons, which can lead to oxidative stress when produced in excess. This relationship has significant implications for cellular health and overall physiological functions (**Rasool *et al.*,2014**).

When potassium dichromate enters the body, particularly through exposure routes such as inhalation, ingestion, or skin contact, it can undergo metabolic processes that result in the release of hexavalent chromium. Hexavalent chromium is a potent oxidizing agent, capable of inducing oxidative stress by promoting the generation of free radicals, such as reactive oxygen species (ROS) (**Liu and Shi, 2001**).

The excessive production of free radicals can overwhelm the body's natural antioxidant defenses, leading to cellular damage, lipid peroxidation, and DNA mutations. This oxidative stress is associated with various adverse health effects, including inflammation, tissue damage, and an increased risk of chronic diseases (**Ibrahima *et al.*,2018**).

Potassium dichromate-induced free radical generation has been extensively studied in both in vitro and in vivo models. The compound's ability to initiate oxidative stress is implicated in its toxicological effects on different organs and systems, including the respiratory, gastrointestinal, and reproductive systems (**Mary Momo *et al.*,2019**).

Understanding the relationship between potassium dichromate and free radical generation is crucial for assessing the compound's overall impact on

cellular health and its potential contribution to various health conditions. Mitigating exposure to potassium dichromate and implementing antioxidant strategies may be essential in minimizing the risk of oxidative stress-related damage in the body (**Jeber and Tawfeek, 2013**).

## 2.3 Ginseng :

Ginseng, a perennial plant belonging to the Panax genus, has etched its place in the tapestry of traditional medicine and herbal remedies. Over centuries, it has garnered acclaim for its potential health benefits and adaptogenic prowess (**Chen *et al.*,2022**).

The botanical diversity of ginseng encompasses various species, with Panax ginseng (Asian or Korean ginseng) and Panax quinquefolius (American ginseng) standing out as the most renowned. Distinguished by fleshy roots, each housing a unique composition of bioactive compounds, ginseng has become a symbol of herbal excellence (**Choi *et al*.,2020**).

In the realm of traditional uses, ginseng has deep roots in Chinese medicine, where it is revered for promoting vitality, improving overall well-being, and addressing various ailments. Its standing as an adaptogen adds to its allure, with claims of assisting the body in coping with stress and restoring balance (**Ibrahima *et al.*,2018**).

At the heart of ginseng's pharmacological effects are its bioactive components, primarily ginsenosides—triterpene saponins with adaptogenic, anti-inflammatory, and antioxidant properties. These compounds contribute to ginseng's potential health benefits, spanning enhanced energy and stamina, cognitive function support, and immune system fortification (**Dong *et al*.,2021**).

Ginseng's adaptogenic properties make it a valuable ally in helping the body navigate stressors, whether physical, chemical, or biological. Its purported

ability to modulate the hypothalamic-pituitary-adrenal (HPA) axis underscores its role in stress regulation.

While traditional uses have laid the foundation, modern research is delving into ginseng's potential in managing diabetes, improving cardiovascular health, and supporting cancer prevention. Ongoing investigations aim to unravel the mechanisms behind its diverse effects on the body (**Faghani *et al.*,2022**).

Ginseng is available in various forms, from fresh or dried roots to powders, extracts, and supplements. Each form may carry distinct concentrations of active compounds, influencing its effectiveness in different applications (**Ibrahima *et al.*,2018**).

Cautions and considerations accompany the use of ginseng, despite its generally recognized safety. Potential interactions with medications and the need for caution in specific health conditions underscore the importance of informed and mindful consumption. ginseng emerges as a herbal treasure with a storied history and a bounty of potential health benefits. Whether embraced in traditional remedies or explored through modern research, ginseng remains a captivating and holistic approach to well-being and vitality. As the realms of herbal medicine and natural health solutions expand, ginseng continues to command attention as a beacon of botanical excellence (**Jang *et al.*,2011**).

**Figure (2.5) Ginseng Herbal**

## 2.3.1 History of use ginseng

The storied history of ginseng begins over two millennia ago in ancient China, where it was embraced by Traditional Chinese Medicine (TCM). Known as "renshen," meaning "man root" or "essence of the earth," ginseng quickly became a symbol of health and vitality. Its perceived restorative properties and rarity elevated its cultural significance, making it a highly sought-after commodity (**Dong *et al*.,2021**).

As its influence spread, ginseng found a home in Korean and Japanese traditional medicine. The Korean peninsula, in particular, gained renown for producing high-quality ginseng, with Korean ginseng earning a reputation for its potency (**Kim *et al.*,2011**).

The introduction of ginseng to the Western world occurred through trade routes, capturing the attention of European explorers and herbalists. Its

remarkable properties led to its incorporation into Western herbalism and alternative medicine.

In Native American practices, American ginseng (Panax quinquefolius) became a valued component of traditional medicine. Indigenous communities recognized its diverse applications and incorporated it into their healing practices (**Kopalli *et al.*,2019**).

Efforts to cultivate ginseng outside its native habitats arose with increasing demand. Conservation initiatives were also introduced to protect wild ginseng populations, ensuring sustainability and preventing overharvesting (**Dong *et al*.,2021**).

Ginseng's reputation continued to grow globally, leading to widespread recognition and commercialization. Today, it is a staple in herbal supplements, traditional medicines, and various wellness products around the world (**Kopalli *et al.*,2016**).

## 2.3.2 Composition of ginseng

Ginseng, a revered herb celebrated for its therapeutic properties, boasts a rich and intricate composition of bioactive compounds that underlie its health-promoting effects (**Park *et al*.,2017**).

At the heart of ginseng's potency are ginsenosides, triterpene glycosides that constitute its primary active compounds. These ginsenosides, including types like Rb1, Rg1, and others, play a pivotal role in endowing ginseng with its adaptogenic, anti-inflammatory, and antioxidant properties. Beyond ginsenosides, ginseng reveals a presence of polysaccharides, complex carbohydrates known for their immune-modulating effects. These compounds contribute to the herb's ability to support the immune system and overall health (**Liu *et al.*,2020**).

Bioactive peptides, short chains of amino acids, are also found in ginseng. These peptides may exert various physiological effects, adding to the overall health benefits associated with ginseng consumption (**Dong *et al*.,2021**).

Polyacetylenes, known for their anti-inflammatory properties, are part of ginseng's composition, contributing to its ability to modulate the immune response. Polyphenolic compounds, with antioxidant properties, are present in ginseng, helping neutralize free radicals and providing cellular protection against oxidative stress (**Majid, 2019**).

Essential oils in ginseng roots contribute to its aroma and may offer additional health benefits. These volatile compounds add to the overall chemical profile of ginseng. Nitrogenous compounds, including amino acids, enrich the nutritional content of ginseng. Amino acids, as fundamental components of proteins, play essential roles in various physiological functions (**Park *et al*.,2017**).

Ginseng also offers a spectrum of vitamins, including B vitamins (B1, B2, B12) and vitamin C. Essential minerals like iron, manganese, and copper further contribute to the herb's nutritional value. In addition to these components, ginseng houses various phytochemicals such as flavonoids, lignans, and coumarins, each adding to the diverse and holistic chemical composition of this herbal treasure (**Choi *et al*.,2019**).

The composition of ginseng is a symphony of bioactive compounds working in harmony. From ginsenosides and polysaccharides to peptides, polyacetylenes, and essential oils, ginseng's multifaceted effects on human health stem from the intricate interplay of its diverse constituents (**Nuri *et al*.,2016**).

## 2.3.3 Medical use of ginseng

Ginseng, deeply rooted in traditional medicine, has transcended cultural boundaries to become a globally recognized herbal remedy with a spectrum of potential health benefits. Its extensive use in medical contexts spans various cultures and traditional healing systems, contributing to its reputation as a versatile and holistic herbal ally (**Choi *et al.*,2019**).

In the realm of adaptogenic properties, ginseng stands as a revered botanical. It is celebrated for its capacity to help the body adapt to stressors, offering both physical and mental resilience. By modulating the body's stress response, ginseng is believed to promote an overall sense of well-being. A hallmark of ginseng's traditional use is its role in enhancing energy levels and combating fatigue. Widely regarded as a natural energizer, ginseng has been employed to promote vitality and endurance, making it a valuable ally in combating physical exhaustion (**De Andrade *et al.*,2007**).

Research suggests that ginseng may extend its benefits to cognitive function, showing potential cognitive-enhancing effects such as improvements in memory and concentration. Its neuroprotective properties position it as a subject of interest in the realm of cognitive health. Beyond its role in personal vitality, ginseng is believed to support the immune system, offering potential protection against infections. Its immune-modulating effects have been traditionally harnessed for preventive health practices (**Park *et al.*,2019**).

The anti-inflammatory properties of ginseng are recognized in traditional medicine, making it a candidate for addressing inflammatory conditions and promoting overall well-being. The rich content of antioxidants, including ginsenosides, contributes to cellular health and protection against oxidative stress Fig.(2.6) has shown that ethanol and methanol extracts of ginseng leaves have the potential to scavenge free radicals **(Ratan *et al*.,2021).**

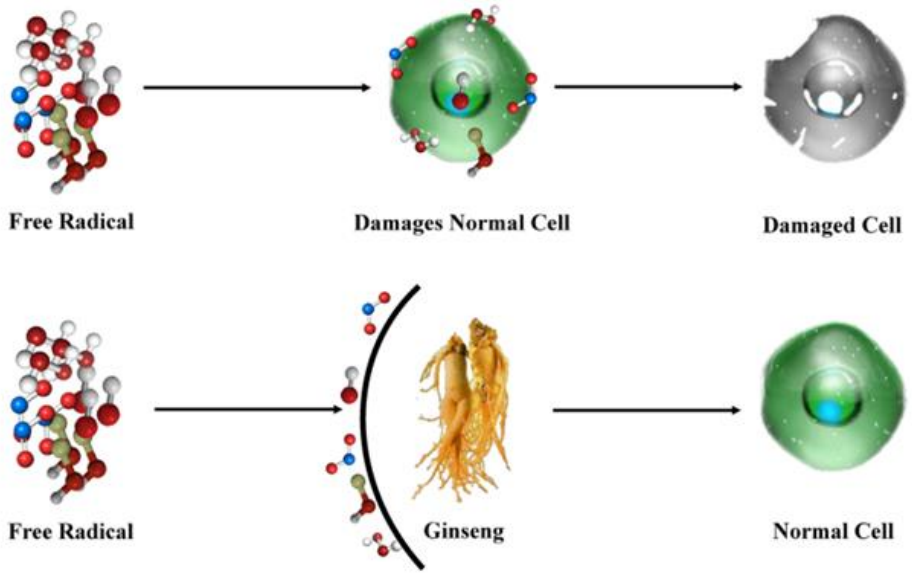



**Figure (2.6) Free radical scavenging activity of ginseng as an antioxidant. (Ratan *et al.*,2021)**

In cardiovascular health, studies suggest that ginseng may have positive effects, potentially regulating blood pressure and supporting overall heart function. Its potential role in managing diabetes is another area of exploration, with indications of improved blood sugar control and insulin sensitivity (**Seghinsara *et al.*,2019**).

Ginseng's potential anti-cancer effects have garnered attention in research, showing inhibitory effects on the growth of certain cancer cells. While more research is needed, this aspect underscores the multifaceted nature of ginseng's potential applications(**Deng *et al.*,2023**).

Traditionally, ginseng has been associated with improving sexual function and libido, contributing to its use in addressing issues related to sexual health. Additionally, its adaptogenic and antioxidant properties position ginseng as a traditional anti-aging remedy, believed to promote longevity and overall well-being (**Goda *et al.*,2008**).

While ginseng's traditional uses are deeply ingrained, it is crucial to approach its medical use with caution. Individual responses can vary, and consulting healthcare professionals is advisable, especially for those with underlying health conditions or those taking medications. Ginseng's holistic properties continue to make it a fascinating subject of research, offering potential contributions to integrative healthcare practices (**Marouani *et al.*, 2012**).

In the realm of exploring complementary approaches for infertility, ginseng, a revered herb in traditional medicine, has emerged as a subject of interest. Navigating the nuanced landscape of herbal remedies necessitates a careful and informed approach, particularly when considering ginseng as a potential ally in infertility treatment **(Ratan *et al.*,2021).**

Ginseng is available in diverse forms, ranging from raw roots to dried roots, extracts, and supplements. Choosing the form that aligns with personal preferences and health needs is a crucial consideration. Determining the right dosage is a nuanced process influenced by factors such as age, health status, and the specific form of ginseng being used. Starting with a modest dose and gradually adjusting while vigilantly monitoring for any adverse effects is a prudent approach (**Zhang *et al.*,2021**).

The timing of ginseng consumption can be tailored to individual preferences. Some individuals may opt for morning consumption to leverage its potential energy-boosting effects, while others may find the afternoon more suitable(**Van Wyk,2019**).

Incorporating ginseng into the diet offers a versatile approach. Whether added to teas, soups, or taken as a supplement, ginseng's adaptability allows for a seamless integration into various dietary routines. Ginseng tea, in particular, has gained popularity for its accessibility and palatability (**Zheng, 2018**).

Consistency in usage is a fundamental principle when considering ginseng for infertility. Regular and sustained use may be necessary to observe potential benefits, and abrupt discontinuation without professional guidance is discouraged.

If both partners are actively involved in fertility treatments, a collaborative approach to incorporating ginseng may be considered. Shared lifestyle changes and mutual support can positively impact the fertility journey.Ginseng should be viewed as a complementary approach rather than a replacement for conventional medical treatments for infertility. Effective communication with healthcare providers ensures that ginseng aligns harmoniously with the overall treatment plan (**Choi *et al.*,2019**).

Patience is a virtue in the realm of herbal remedies. Recognizing that results may vary among individuals and that herbal interventions may take time to manifest effects is an essential mindset. The unique responses to ginseng underscore the importance of tailoring the approach based on individual needs and health conditions **(Ratan *et al*.,2021)**

The narrative guide to using ginseng for infertility treatment underscores the importance of a thoughtful and informed approach. Professional guidance, consistent monitoring, and an individualized strategy are pivotal components of this holistic and safe journey toward potential fertility support (**Park *et al.*,2019**).

# Chapter Three

# Methodology

# 3. Materials and methods

## 3.1. Materials

### 3.1.1 Chemicals and Kits:

All chemical materials, purified reagents and standard kits that are used in this study with their origin are listed in tables (3-1) and (3-2) respectively below.

**Table (3-1): Chemical, Manufacture and Source Country.**

| NO. | Chemicals | Manufacture | Country |
|---|---|---|---|
| 1 | Chloroform | Bio Chemika | Germany |
| 2 | Eosin-hematoxylin stain | Merck | Germany |
| 3 | Ethanol | Merk | Germany |
| 4 | Formalin | BDH | England |
| 5 | Ginsing | Local | China |
| 6 | Methanol | GCC | England |
| 7 | Potassium dichromate | Qualkems | India |
| 8 | Selenium | Merck | USA |

**Table (3-2): Standard Kits with their Suppliers**

| NO. | Kit | Supplied company | Country |
|---|---|---|---|
| 1 | Anti-luteinizig hormone antibody (LH-AB) ELISA Kit | sunlong | China |
| 2 | Catalase (cat) Spectrophotometer kit | solarbio | China |
| 3 | dihydrotestesterone (DHT) ELISA Kit | sunlong | China |
| 4 | Follicle Stimulating Hormone (FSH) ELISA Kit | sunlong | China |
| 5 | Malondialdehyde(MDA) Spectrophotometer kit | solarbio | China |
| 6 | Superoxide Dismutase(SOD) Spectrophotometer kit | solarbio | China |

### 3.1.2. Instruments and Equipments:

The study's equipment and instruments that were utilized in the investigations of the current study (Chapter Three Materials and Methods) are listed and described with their full details (company, city, and country) in the table 3-3, below.

**Table (3-3): Instruments, Manufacture and Country Sources.**

| NO. | Instrument | Manufacture | Country |
|---|---|---|---|
| 1 | Anatomical set (Scissors, Forceps, Scalpe | Chemo lab | China |
| 2 | Beakers (100, 250, 500, 1000) | Chemo lab | India |
| 3 | Camera Digital | Sony | Japan |
| 4 | Centrifuge | Hettich Roto fix11 | Japan |
| 5 | Microplate Reader "Asys Expert 96" | Biochrom | USA |
| 6 | Embedding center | Leed | China |
| 7 | Incubator | Nuve | Japan |
| 8 | Micropipette | Dragon | China |
| 9 | UV-visible spectrophotometer | Shimadzu | Japan |
| 10 | Microscopic | Olympus | Japan |
| 11 | Water Bath | WNB | Belgium |
| 12 | Microplate Elisa Reader | Biotelk | USA |
| 13 | Microplate ElisaWashe | Biotelk | USA |
| 14 | Electronic Balance | Metter company | Switzerland |
| 15 | Electronic microscope | Hitachi | Japan |
| 16 | Graduated Tube | Chemo lab | India |
| 17 | Fourier-transform infrared spectroscopy (FTIR) | Shimadzu corporation | Japan |
| 18 | Scanning electron microscope (SEM) | ZEISS | Germany |
| 19 | X-ray diffraction | Shimadzu | Japan |

## 3.2 Methods:

### 3.2.1 Animal Management:

The present study was conducted in the college of Veterinary medicine – at University of Kerbala, in the animal house of the department of physiology. A total number of 42 male adult albino rats (*Rattus*), with an average weight between (200±20g) and the ages of animals were ranged (from 8 to 10) weeks, were used in the current study. They were housed for two weeks for an adaptation before the experiment. Every six animals were housed in an individual plastic cage measured as 15x35x50cm. They were fed *ad libitum* with the meal of standard pellet of diet supplied from IPA (Institute for Public

Accuracy), counter for agriculture research. They had free access to water to drink, and they were kept under the exact condition of temperature (22-25) C° and light, the regime of 14hours of light, and 10 hours, of darkness. At the beginning of the experiment, the initial body weight of adult rats was recorded and then obtained until the end of the investigation; body weight gain was also recorded.

### 3.2.2 The Experiments Design

Animals in the study were divided into seven groups. Each group consists of 6 male rats used for the design experiments as the following .

1- Group-1(Control Negative Group): Animals received orally normal saline, daily for four weeks.

2- Group 2 Animals (Potassium Dichromate Group): received Potassium Dichromate 2 mg/kg of body weight daily, intraperitoneally for 2 weeks(**Akinwumi *et al.*, 2016**) .

3- Group 3 (Ginseng Group): Animals received ginseng orally at a dose (200 mg/kg b.wt.) daily for four weeks(**Abo-Raya *et al.*, 2013**).

4- Group 4 Animals (Nano ginseng) Animals received Nano-ginseng orally at a dose (200 mg/kg b.wt) daily for four weeks daily .

5- Group 5 Animals: animals were administered a mixture of potassium dichromate (2 mg/kg) and ginseng (200 mg/kg) orally daily for 4 weeks. During this period, potassium dichromate was discontinued after only two weeks, while ginseng was continued alone for the entire 4 weeks.

6- Group 6 Animals: received Potassium Dichromate + ginseng -NPs at a dose (200 mg/kg b.wt) daily for 4 weeks.During this period, potassium dichromate was discontinued after only two weeks, while ginseng-NPs was continued alone for the entire 4 weeks

7- Group 7 Animals: received Potassium Dichromate + ginseng -NPs at a dose (100 mg/kg b.wt) daily for 4 weeks . During this period, potassium dichromate

was discontinued after only two weeks, while ginseng-NPs was continued alone for the entire 4 weeks.

## 3.3 Ethical approve

Under the reference number UOK.VET.PH.2024.046, this research was carried out in the anatomical laboratory of the College of Veterinary Medicine at the University of Kerbala – Iraq.

## 3.4. Chemicals preparations

### 3.4.1 potassium dichromate Preparation:

In this experiment, each rat was administered 0.4 mg of potassium dichromate (prepared as a 0.4 mg/ml solution) intraperitoneally on a daily basis for two weeks.

### 3.4.2 Preparation of Alcoholic extraction of ginseng

The air-dried ground ginseng material (100 g for sample) was extracted according to the (**Sultana *et al.*,2009**), with the solvent aqueous methanol (methanol: water, 80 % v/v) (500 ml) for 8 hours under Soxhlet on a water bath in separate experiments. With the use of a rotary evaporator, the extracts were concentrated and freed of solvent under reduced pressure at 45 °C. The dried crude concentrated extracts were weighed to calculate the yield and stored in a refrigerator 4C until used **(Sultana *et al.*,2009**).

### 3.4.3 Biosynthesis of Selenium nanoparticles (Se-NPs).

Ginseng plant extract was used for the green biosynthesis Se-NPs through the eco-friendly method. Plant extract 10 ml was added to 90 ml of 2 mM Na2SeO3, where a combination was prepared. For the control sample, 10 ml of D.W was added to 90 ml of 2 mM Na2SeO3. Both flasks were incubated in the rotary shaker for 3 h in the dark to obtain a homogenous mixture. The generated Se-NPs were then separated and purified using D.W and centrifugation. Dried Se-NPs were stored at room temperature for further analyses (**Salem *et al.*,2022**).

## 3.4.4 Characterization of Nanoparticles:

These characterization tests were done in the material research laboratories at the ministry of sciences and technology environment and water research and technology director (EWRTD).

### 3.4.4.1. UV-VIS Spectrophotometer

The stability and production of Ginseng nanoparticles were studied using a double beam (labored). Spectrophotometers with wavelengths ranging from (200 – to 800 ) nm. The solution was measured at the wavelength (of 480 ) nm **(Amendola *et al.*, 2010)( Olteanu *et al.*, 2017 ).**

### 3.4.4.2 Fourier Transform Infrared (FTIR Analysis)

Fourier-transform infrared (FTIR) spectroscopy is the most practical method for identifying chemicals based on the presence of functional groups or interactions between them. Organic and inorganic chemicals in an unknown combination were analyzed using FTIR (Shimadzu) in solid, liquid, and gaseous forms. FTIR is based on the observation that most molecules absorb light in the infrared region of the electromagnetic spectrum. It turns data from the interference pattern into a spectrum **(Choudhary *et al.*, 2019)** by measuring the frequency as wave numbers, which are generally in the range of 400–4000 cm. For the characterization of unknown compounds, FTIR is a useful instrument.

### 3.4.4.3 Scanning Electron Microscopy (SEM) Observation

The scanning electron microscope (SEM) was utilized to examine the NPs' surface morphology. This test and all characterizations of biogenic Nano Ginseng were performed at the Ministry of Science and Technology. This energy is lost as a variety of signals when the electrons are decelerated by their contacts with the material in a SEM. Accelerated electrons in a SEM carry a substantial amount of kinetic energy. X-Ray, visible light, heat, and secondary

electrons are some of the other signs that may be detected. Imaging samples is often done with the use of secondary electrons and backscattered electrons. Secondary electrons are best for revealing sample morphology and topography, while backscattered electrons are better for showing chemical differences in multiphase samples. Elemental and crystalline structural analyses are performed using X-rays **(Kumar,2021).** With the use of electron microscopy, the nanoparticles' size, shape, and surface morphology may be determined. There are several benefits in using scanning electron microscopy for morphological and size analyses. However, they do not provide an accurate picture of the population's size dispersion or genuine average. To begin the SEM characterization procedure, a dry powder made from a solution of nanoparticles is required. A sample container is then used to hold this dry powder (**Tiwari *et al.*, 2021**).

### 3.4.4.4 The X-ray Diffraction (XRD) Measurement

The X-ray diffraction (XRD) analysis was performed using an XRD system (Phillips PW 1830) operated at a voltage of 40 kV and current of 20 mA to determine the crystallinity, metallic nature, and cubic structure of the tested samples. Analysis was carried out in the department of Materials Research, Ministry of Science and Technology, Iraq (**Hateet *et al.*, 2021**).

## 3.5 Blood & Samples Collection:

In all of the studies, rats were sacrificed at the end of the treatment period during the 45 days experiment. The controlled and treated animals, before sacrificing, were initially put to anaesthetised with diethyl ether an anesthesia using cotton swabs in a covered container. The chest and the abdominal cavities were widely opened to give a clear view of the reproductive organs (testis, epididymis) needed in the studies. The blood was drawn using the **Hoff and Ralatg, (2000)** technique of cardiac puncture. A 5ml disposable syringe was

used to draw blood from the heart using the non-heparinized plane tube, which was then centrifuged for 15 minutes at (3000 rpm) to extract the serum, which was then transferred to epndroffe tubes and kept at (-20C) until all tests were completed.

## 3.6 Hormones Assay

Assay for Hormones (ELISA) Testosterone, Follicular Stimulating Hormone (FSH), and Luteinizing Hormone (LH). The premise behind enzyme-linked immunosorbents is that an enzyme is used to detect antigen-antibody binding. Using a colorless substrate, the enzyme creates a brightly colored end product, showing the incidence of Ag: Ab binding (**Ma, and Shieh 2006**).

### 3.6.1Estimation of Testosterone Hormone (T) Concentration (ng/ml).

Serum testosterone hormone(T) concentration in the current study was measured by ELISA technique using commercial test kit as listed in (Table 3-2). Uses a biotin double antibody sandwich technology-based enzyme-linked immunosorbent assay (ELISA) to measure Testosterones levels in samples (**Mujika *et al.*, 1996**). testing procedure was according the manufacturer's instruction as illustrated in appendix I.

### 3.6.2 Estimation of Follicular Stimulating Hormone (FSH) Concentration (mlU/ml).

Serum follicle stimulating hormone concentration in the current study was measured by ELISA technique using commercial test kit as listed in (Table 3-2). Uses a biotin double antibody sandwich technology based enzyme-linked immunosorbent assay (ELISA) to measure FSH levels in samples (**Di-Simoni *et al.*, 1997**), testing procedure was according the manufacturer's instruction as illustrated in appendix II.

### 3.6.3 Estimation of Luteinizing Hormone (LH) Concentration (ng/ml).

Serum Luteinizing hormone concentration in the current study was measured by ELISA technique using commercial test kit as listed in (Table 3-2). uses a biotin double antibody sandwich technology-based enzyme-linked immunosorbent assay (ELISA) to measure LH levels in samples (**Uotila *et al.*, 1981**), testing procedure was according the manufacturer's instruction as illustrated in appendix III.

## 3.7 The Oxidant and Anti-oxidant Parameter:

### 3.7.1 Serum Malondialdehyde Measurement (MDA)

The ability to accurately measure lipid peroxidation in disease states necessitates this method of assessing oxidative stress. MDA and 4 hydroxynonenal (4-HNE) are the natural bi-products of lipid peroxidation. One of the most commonly acknowledged methods for assessing oxidative damage is to measure the lipid peroxidation products. It is easy to use the MDA Microplate Assay Kit to detect MDA in a range of samples. Thiobarbituric Acid (TBA) reacts with MDA in the sample to form the MDA-TBA adduct. You may readily measure the MDA-TBA adduct using a colorimeter ( $\lambda$= 532 nm), according to **Kavsak, (2017)** ,as illustrated in the appendix IV.

### 3.7.2 Superoxide Dismutase (SOD) Activity.

Dismutation of superoxide radicals (O2-) into hydrogen peroxide (H2O2) and elemental oxygen (O2) is catalysed by superoxide dismutases (SODs), which act as a crucial defence against superoxide radical toxicity. Tumor cells are protected from apoptosis in mice lacking SOD1 and SOD2, however these animals spontaneously acquire liver cancer. NBT is converted to NBT-diformazan by xanthine oxidase (XOD) and hydrogen peroxide in the

Superoxide Dismutase Microplate Assay Kit. Light with a wavelength of 560 nm or longer is absorbed by NBT-diformazan. SODs diminish the levels of superoxide ions, which in turn reduce the rate at which NBT-diformazan is formed. NBT diformazan decrease is a good indicator of SOD activity in experimental samples, according to (**Kavsak, 2017**) In Appendix V.

### 3.7.3 Catalase activity

This kit is an Enzyme-Linked Immunosorbent Assay (ELISA). The plate has been pre-coated with Rat CAT antibody. CAT present in the sample is added and binds to antibodies coated on the wells. And then biotinylated Rat CAT Antibody is added and binds to CAT in the sample. Then Streptavidin-HRP is added and binds to the Biotinylated CAT antibody. After incubation unbound Streptavidin-HRP is washed away during a washing step. Substrate solution is then added and color develops in proportion to the amount of Rat CAT. The reaction is terminated by addition of acidic stop solution and absorbance is measured at 450 nm(**Fauss *et al.*,2013**). Appendix VI

## 3.8 Organs :

Testes and epididymis were collected from each animal and fixed in 10% formalin for the preparation of slide to investigate the histopathological changes in both the control and treated groups.

### 3.8.1 Histological Studies

The testes were collected from all studied groups to prepare slides for a histological examination according (**meschar, *et.al.*,2010**) with the used of the light microscope as the following steps:

1. Fixation: The fixation for 48 hours in formalin solution.

2. Dehydration: The histological specimens were passed in the serial concentrations for the period two hours for each concentration of ethyl alcohol, starting from (80%, 90%, 95%, 100%).

3. Clearing To removed alcohol xylene was used on the histological specimens for period time inhalf hour –twicely.

4. Infiltration. After clearing put the histological specimens in a mixture of xylene and paraffin wax melted and the degree of melting 58-56C° for 15 minutes in an electric oven temperature 60C°, and then turned to a new wax fusible only and put in the oven for a period ranging between an hour and a half to two hours.

5. Embedding The histological specimens embedded in the same quality of wax used in the infiltration process and the work of which cubic waxy templates, and then left to harden and then trimmed and glued wooden cubes cube and equipped to cut.

6.Sectioning:The histological specimens were cut by the Rotary microtome letizwetzlar, Germany at the thickness, five micrometer, cross sections for each of the testis, and then put the sections on glass slides by using a (Mayer's albumin).

7. Staining :Use Harshaematoxylin and Eosin .

8. Mounting: Destern plastiszer xylin material used for mounting the histological sections on the slides.

## 3.9 Statistical Analysis

The Lilliefors-corrected Kolmogorov-Smirnov test was used to examine the distribution types of the results group. A statistical distribution divides variable results into two types: normally distributed and non-normally distributed

variables. The results of the normally distributed variable were expressed as (mean ± standard deviation). While the results for the non-normally distributed variables were expressed as medians and (25%-75% interquartile). The comparison between normally distributed variables were made by independent samples t-test between two groups. The comparison between three or more groups was caried out by analysis of variance (ANOVA), followed by Tukey's Honestly Significant Difference (HSD) test as a post-hoc analysis to compare between each pair of groups. While the comparison of non-normally distributed variables was made by Mann-Whitney U test.

All statistical tests were two-tailed, and a p-value of 0.05 was used for statistical significance. The tables contain probability values (p) and F-statistic value (F). SPSS Statistics version 26 and IBM-USA performed all statistical analyses. At the same time, the figures would be structured by using Excel Microsoft Office 2021**.**

# Chapter Four
# Results and Discussion

# 4. The Results:

## 4.1. Characterization of Ginseng Nanoparticles (NPs).

Different spectrophotometric techniques like UV-visible, SEM, XRD, and FTIR analysis were used to investigate the morphology, elemental composition, crystalline nature, functional group, and stability of synthesized LCNPs. Details of these techniques are given in chapter 2.

### 4.1.1. UV-Vis Spectroscope:

The optical properties of ginseng extract and functionalized ginseng nanoparticles were investigated using ultraviolet-visible (UV-vis) spectrophotometry.The UV-vis spectra were acquired by scanning the prepared solutions in a UV-visible spectrophotometer over a wavelength range of 200-800 nm.

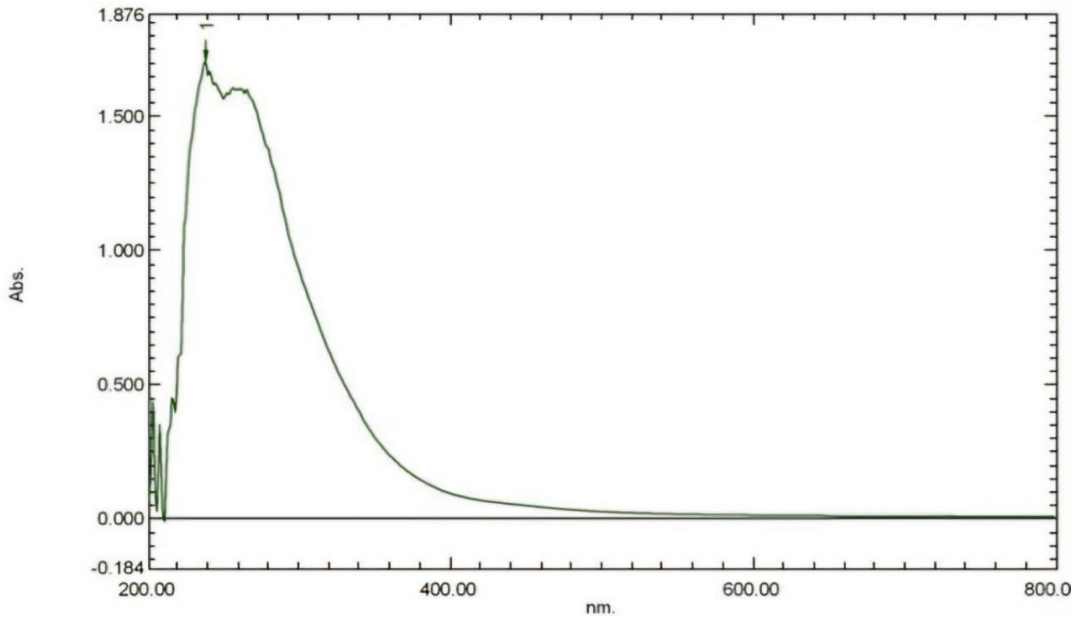



**Figure (4-1) UV-visible spectroscope of Ginseng extract**

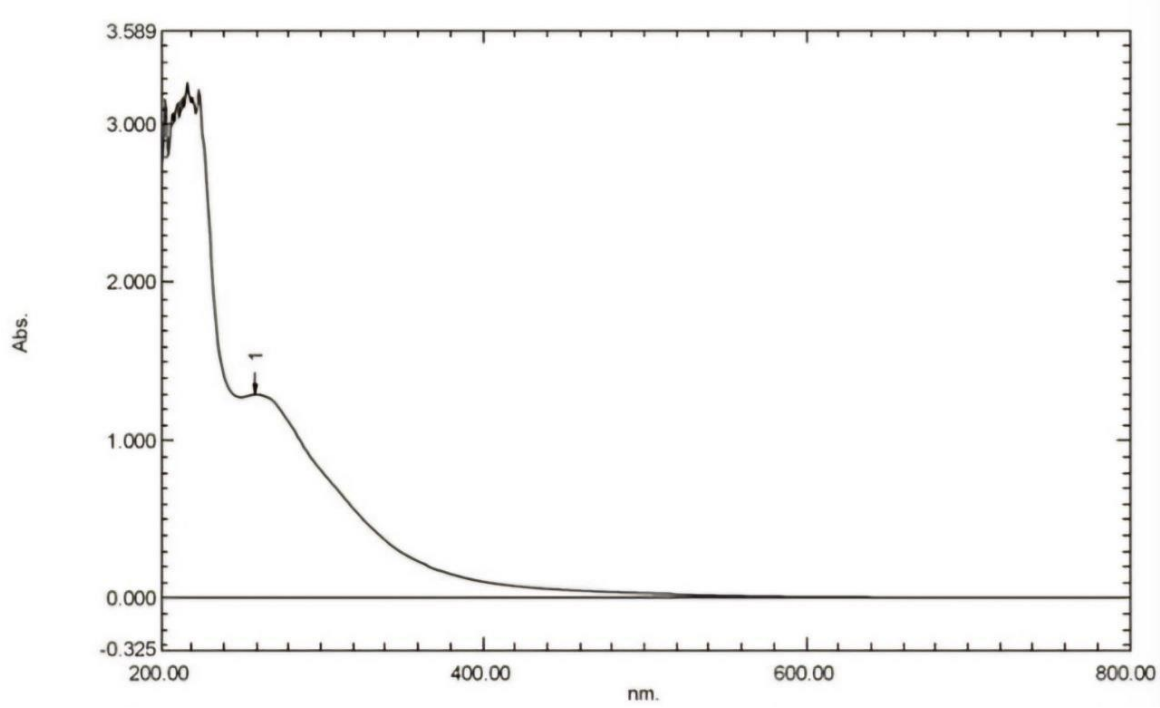



**Figure (4-2) UV-visible spectroscope of Ginseng nanoparticles**

As shown in Figures (4.1) and (4.2), the UV–vis spectra revealed distinct absorption peaks for both the ginseng extract and the functionalized ginseng nanoparticles. The ginseng extract solution showed a distinct absorption peak at 733 nm, which is consistent with the electronic transitions of the ginseng saponin molecules. In contrast, the UV–vis spectrum of the functionalized ginseng nanoparticles presented a prominent absorption peak at 257 nm, which is attributed to the size-dependent light scattering properties of the nanoparticles.

The results of the recent study are consistent with those reported in other studies on the UV properties of ginseng extract and nanoparticles. Specifically, the observed absorption peak of ginseng extract is at 733 nm aligns with the findings of **Pan *et al.* (2010)**, Who attributed this peak to electronic transitions of ginseng saponin molecules. Likewise, the size-dependent light scattering properties of functionalized ginseng nanoparticles, evidenced by the absorption peak at 257 nm, are in line with observations of **Hu *et al.*, (2012**).

## 4.1.2.Fourier Transforms Infrared Spectroscopy Analysis (FTIR):

FTIR spectroscopy can be used to determine the presence of ginsenosides in ginseng extracts. The FTIR spectrum of ginseng extract will show characteristic peaks consistent with the presence of specific ginsenosides. By comparing the FTIR spectrum of a ginseng extract to the reference spectrum, it is possible to determine the types of ginsenosides present in the extract. The region of the spectrum between 3500 and 3000 cm-1 is associated with the presence of hydroxyl groups (-OH). Ginsenosides contain many hydroxyl groups, so this region of the spectrum is typically strong in ginseng extracts.

The spectrum region between 1800 and 1600 cm-1 is associated with the presence of carbonyl groups (C=O). Ginsenosides also contain carbonyl groups, so this region of the spectrum is also strong in ginseng extracts.

The region of the spectrum between 1300 and 1000 cm-1 is associated with the presence of sugars. Ginseng extracts contain sugars, so this area of the spectrum is also strong in ginseng extracts **Wang *et al*., (2020).**

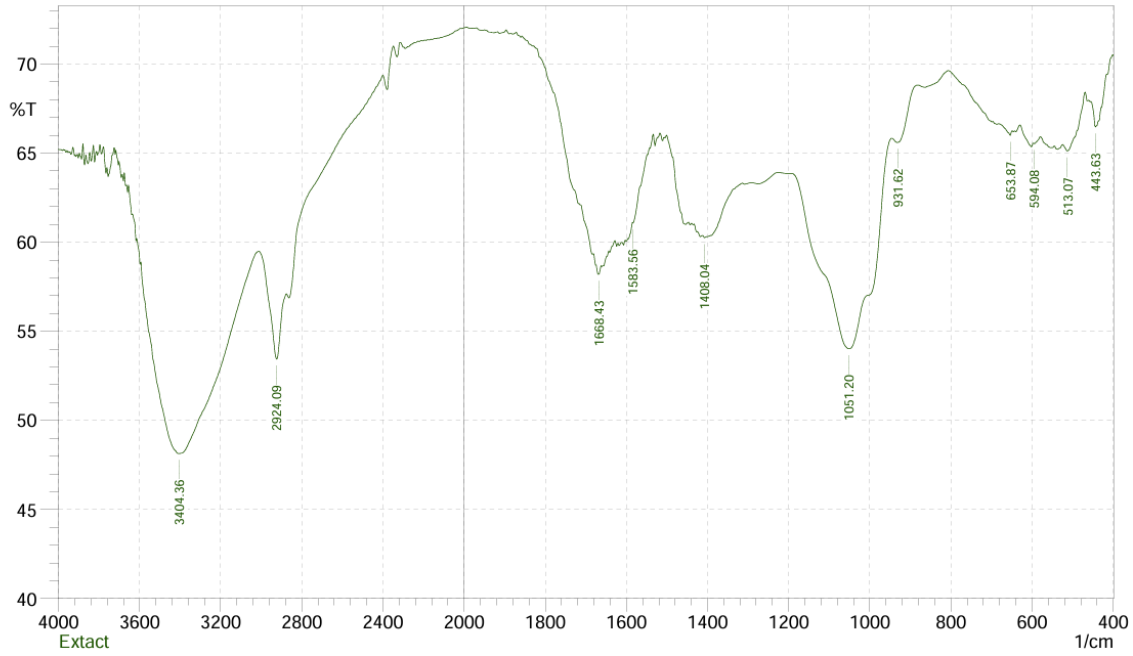



**Figure (4-3) FT-IR spectrum showing functional groups of Ginseng extract**

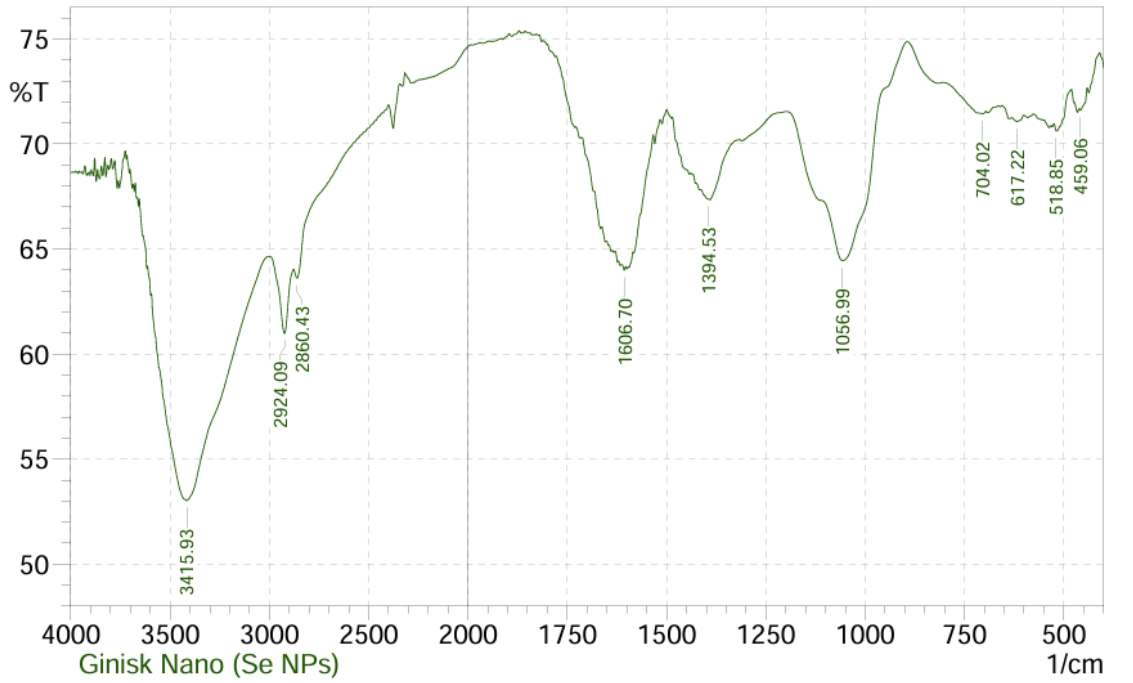



**Figure (4-4) FT-IR spectrum showing functional groups of Ginseng Nanoparticles**

FTIR spectroscopy was used to distinguish between different geographical origins of ginseng based on their ginsenoside profiles. Their study identified distinct peaks corresponding to specific ginsenosides in the regions they highlighted (3500-3000 $cm^{-1}$ for hydroxyl groups, 1800-1600 $cm^{-1}$ for carbonyl groups, and 1300-1000 $cm^{-1}$ for polysaccharides **Lv *et al.*, (2019).**

FTIR analysis has been used along with other techniques to evaluate the quality of ginseng extracts. Their study confirmed the presence of distinct peaks associated with ginsenosides, hydroxyl groups, carbonyl groups, and sugars, aligning with your observations as in the results of **Liu *et al.*, (2018)**. Investigation of the stability of ginsenosides in ginseng extracts under different storage conditions using FTIR spectroscopy. Their study demonstrated the ability of FTIR to monitor changes in functional groups associated with ginsenosides over time. The agreement between recent results and these studies strengthens the validity of using FTIR analysis to characterize ginseng extracts.

### 4.1.3. SEM (Scanning Electron Microscope)

Scanning electron microscope analysis of the prepared nanoparticles and comparison with ginseng extract at different magnification images shows the distribution and size of the nanoparticles as shown in Figure (4.5). The SEM image results show that the ginseng nanoparticles are arranged in a regular circular pattern, with an obvious size difference between the particles. The particle sizes in the image range from 27.69 nanometers to 36.99 nanometers, making them too small to be seen with the naked eye.

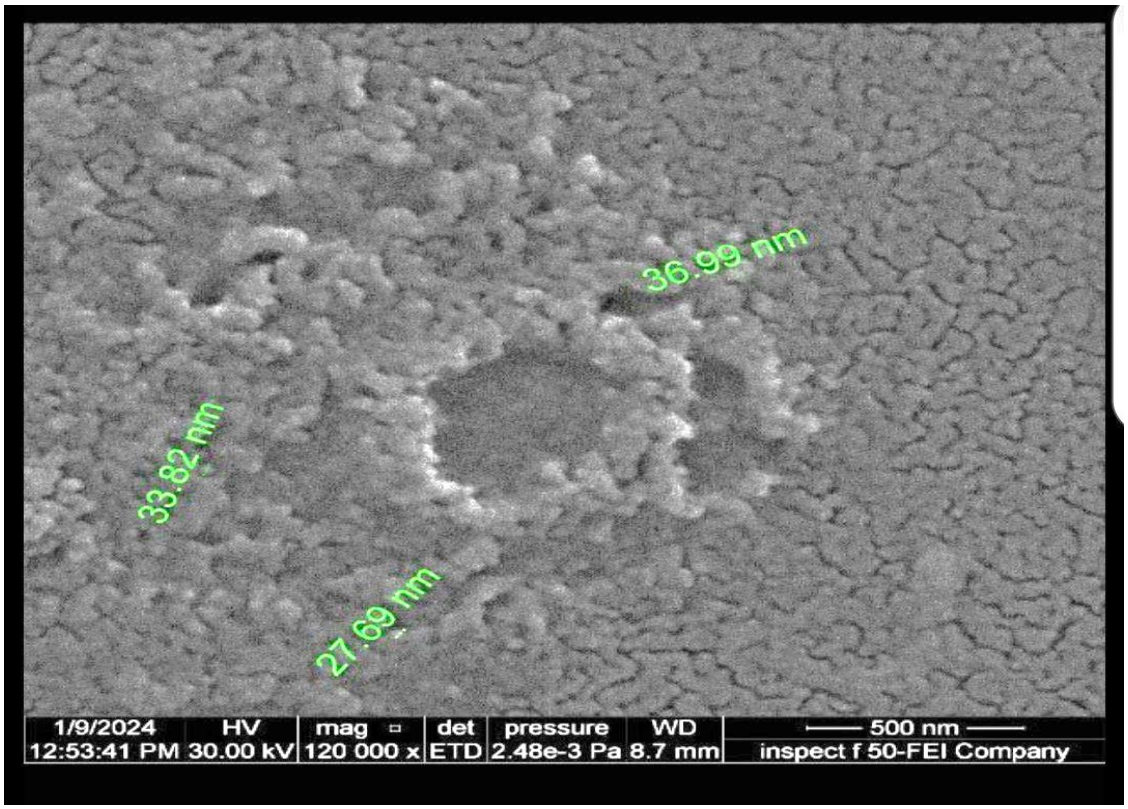



**Figure (4.5) Scanning electron microscopy (SEM) shows the morphology and size of biogenic nanoparticles (NPs).**

Ginseng nanoparticles are characterized by the presence of small pores on their surface. These pores increase the surface area of molecules, enhancing their absorption into the body and improving their ability to deliver their active ingredients. Scanning electron microscope analysis of the prepared nanoparticles showed that ginseng particles are arranged in a regular circular pattern, with obvious size variation between particles. The particle sizes ranged from 27.69 nm to 36.99 nm, which is consistent with previous studies on ginseng nanoparticles using SEM **Kim *et al.*, (2020)**.The presence of spherical nanoparticles with a size ranging between 200-300 nm was observed, while.. **Hu *et al.*, (2012)**. Nanoparticles between 50-100 nm are reported. These differences highlight the effect of preparation methods on particle size.

## 4.1.4. X-Ray Diffraction Analysis (XRD):

The XRD of the prepared ginseng nanoparticles was measured to confirm the results obtained by SEM and to determine the size of the nanoparticles as shown in Figures (4.6). The XRD pattern of ginseng nanoparticles shows several distinct peaks, indicating the presence of a crystalline phase. The locations and intensities of these peaks provide valuable information about the crystal structure of the material.

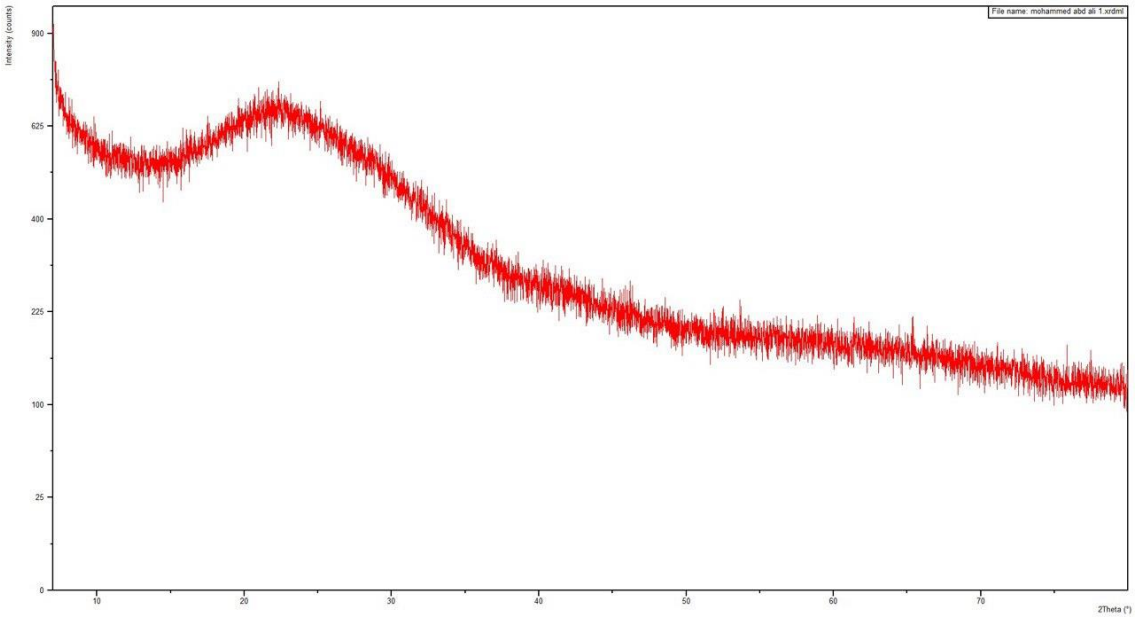



**Figure (4-6): XRD of biosynthesized Ginseng Nanoparticles.**

The crystalline phases present in the sample can be determined by X-ray diffraction (XRD) analysis. In the case of ginseng nanoparticles, the pattern obtained from XRD analysis can indicate the presence of known ginseng crystal phases, such as ginseng saponin crystals. **Kim *et al.*, (2020)** used XRD analysis to examine ginseng nanoparticles loaded with ginsenoside Rg1 and discovered the presence of a specific crystalline phase of ginseng. Similarly**, Zhao *et al.*, (2021)** used XRD analysis to characterize the structural properties of ginseng-loaded nanocarriers, including their crystal phase and crystal size. The results of the recent study are consistent with these studies in using XRD technology to identify a specific crystalline phase of ginseng in ginseng nanoparticle samples.

## 4.2 Toxicity of Dichromate, Ginseng, and ginseng-NP

**Table 4.1. Comparison in the serum biomarkers level in rat after exposure to dichromate (Group 2), ginseng extract (Group 3) and ginseng-nanoparticles (Group 4) with the control group (Group 1)**

| | Group 1 [A] | Group 2 [B] | Group 3 [C] | Group 4 [D] | F | p |
|---|---|---|---|---|---|---|
| **MDA nmol/ml** | 10.3±0.96 [B, C, D] | 14.52±1.12 [A, C, D] | 7.18±1.68 [A,B] | 6.95±1.41 [A,B] | 35.683 | <0.001 |
| **SOD U/ml** | 380.4±39.83 | 254.77±67.46 [C] | 436.4±134.39 [B] | 447±47.24 [B] | 5.890 | 0.007 |
| **Catalase U/ml** | 6.05±0.67 [B] | 4.55±0.76 [A, C, D] | 6.53±0.77 [B] | 7±0.37 [B] | 12.806 | <0.001 |
| **LH-Ab IU/L** | 4.14±0.56 | 2.88±0.67 [C, D] | 5.78±1.51 [B] | 5.91±1.17 [B] | 9.487 | 0.001 |
| **DHT pg/ml** | 342±69.07 [B] | 134.2±42.04 [A, C, D] | 383±22.93 [B] | 386.8±28.19 [B] | 36.604 | <0.001 |
| **FSH ng/ml** | 22.7±2.08 [B, C, D] | 15.15±2.19 [A, C, D] | 29.02±3.37 [A,B] | 29±3.29 [A,B] | 27.735 | <0.001 |

**[A]: Comparison with control group (Group 1), [B]: Comparison with the dichromate treated group (Group 2), [C]: Comparison with ginseng treated group (Group 3), [D]: Comparison with ginseng-nanoparticles treated group (Group 4). MDA: malondialdehyde, SOD: Superoxide dismutase, LH-Ab: Antibodies against luteinizing hormone, DHT: Dihydrotestosterone, FSH: Follicular-stimulating hormone.**
**p-value of 0.05 was used for statistical significance,(p)= probability values and (F)= F-statistic value**

Serum SOD is significantly increased in Groups 3 and 4 compared with the Group 2. Serum catalase level is significant in Group 2 compared with other groups (Groups 1, 3, and 4). The level of LH-Ab is significant in Groups 3 and 4 compared with Group 2. Serum DHT level is significant in Group 2 compared with other groups (Groups 1, 3, and 4). Serum FSH in Groups 3 and 4 is significant than the Groups 1 and 2. As shown in figures below .

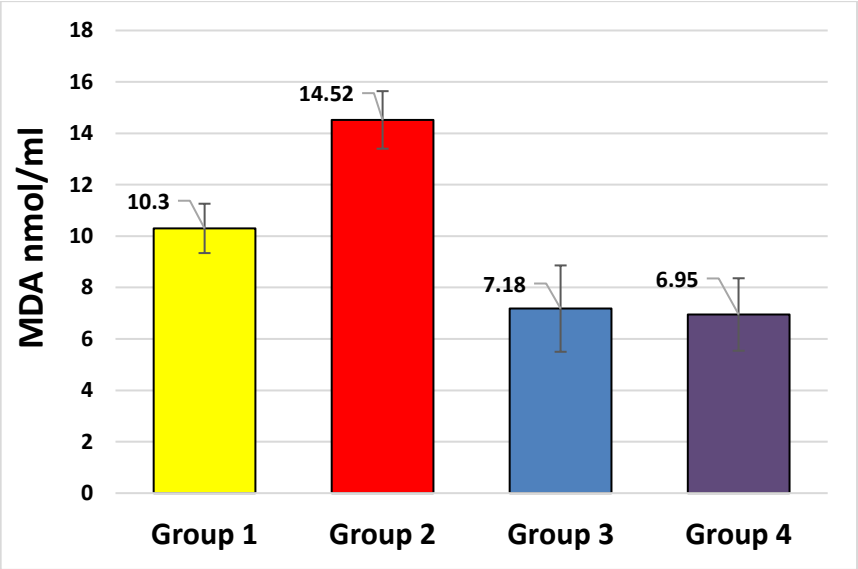



**Figure (4.7) Comparison of serum malondialdehyde (MDA) level in rat after exposure to dichromate (Group 2), ginseng extract (Group 3) and ginseng-nanoparticles (Group 4) with the control group (Group 1)**

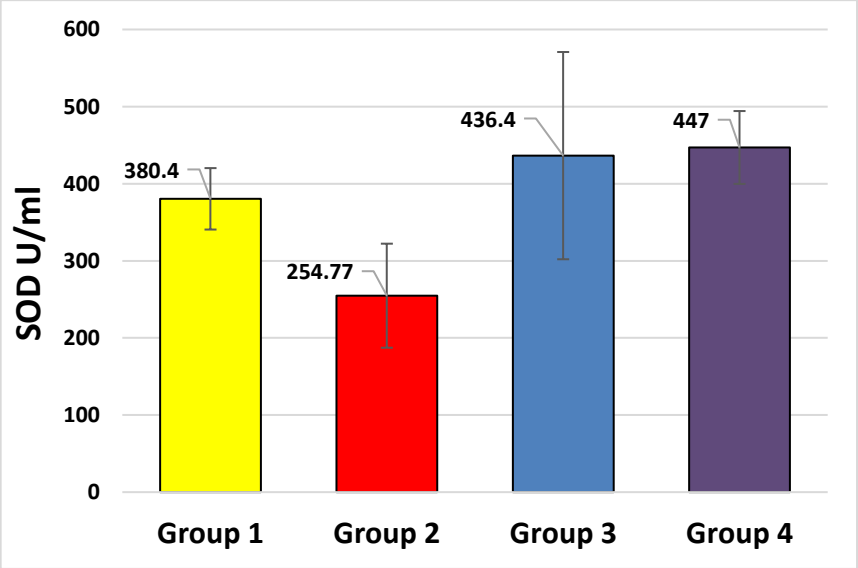



**Figure (4.8) Comparison of serum superoxide dismutase (SOD) activity in rat after exposure to dichromate (Group 2), ginseng extract (Group 3) and ginseng-nanoparticles (Group 4) with the control group (Group 1)**

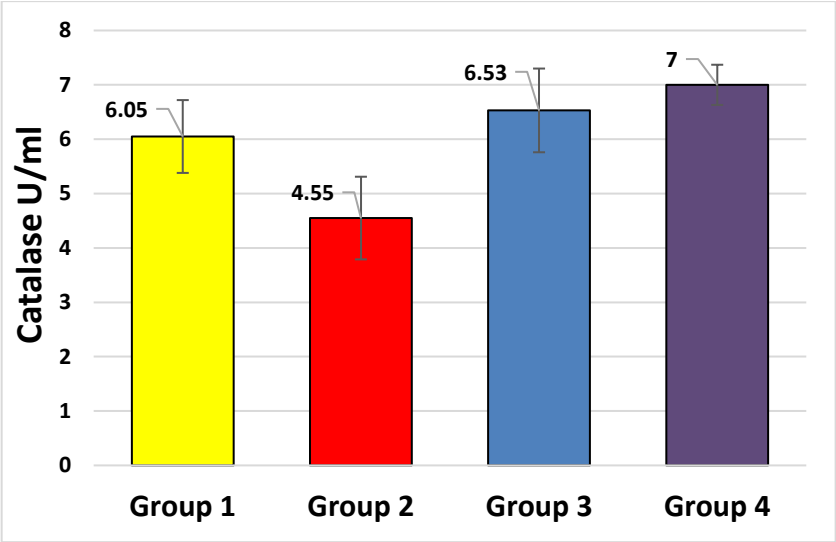



**Figure (4.9 )Comparison of serum catalase activity in rat after exposure to dichromate (Group 2), ginseng extract (Group 3) and ginseng-nanoparticles (Group 4) with the control group (Group 1)**

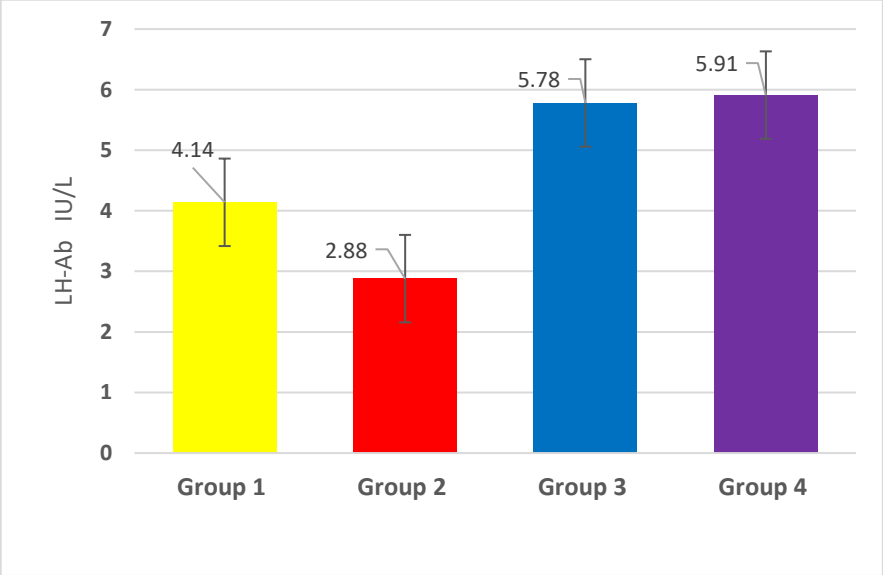



**Figure (4.10): Comparison of serum luteinizing hormone antibodies (LH-Ab) level in rat after exposure to dichromate (Group 2), ginseng extract (Group 3) and ginseng-nanoparticles (Group 4) with the control group (Group 1)**

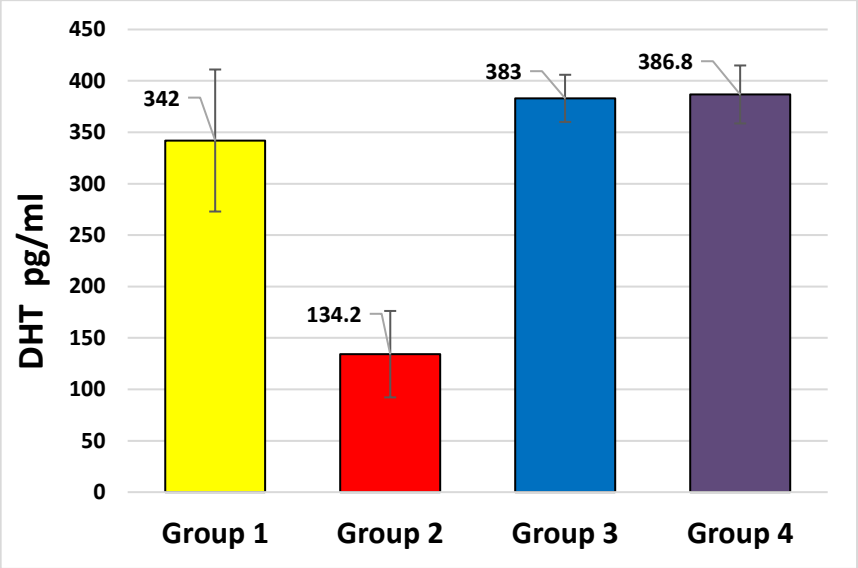



**Figure (4.11) Comparison of serum dihydrotestosterone (DHT) level in rat after exposure to dichromate (Group 2), ginseng extract (Group 3) and ginseng-nanoparticles (Group 4) with the control group (Group1)**

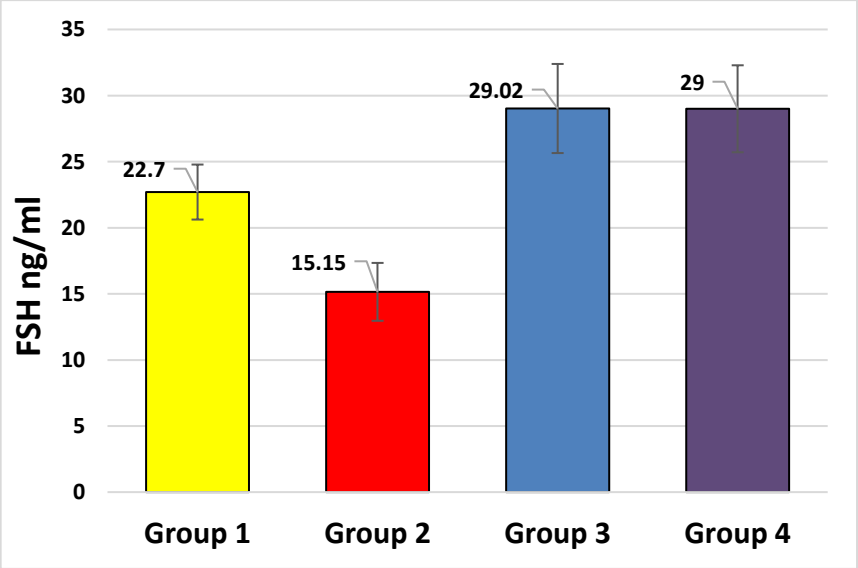



**Figure (4.12). Comparison of serum Follicular-stimulating hormone (FSH) level in rats after exposure to dichromate (Group 2), ginseng extract (Group 3) and ginseng-nanoparticles (Group 4) with the control group (Group 1)**

The first major finding of this study is the reduction of MDA after toxicity by PDC and its reduction after treatment with ginseng extract and ginseng-NPs suggesting a protective effect of these ginseng preparations on PDC toxicity in rats. Ginseng preparation also increases hormone levels (FSH and DTH) and antioxidants (SOD and catalase enzyme levels), as well as LH-Ab levels as shown in Table (4.1). These results are important for the use of ginseng as a toxicity agent protection in animal models.

Previous studies have shown that adding ginseng is beneficial in reducing the effect of nicotine toxicity. FSH and LH levels were significantly increased after treatment with nicotine plus ginseng (**Faghani *et al.*, 2022**)( **Emmanuel *et al.*, 2017**).

Furthermore, the combination of nicotine and ginseng treatment showed a reduction in tissue MDA levels and an increase in SOD compared to the nicotine group. This was reported by **Faghani *et al.*, (2022)**. This type is able to increase testosterone by directly affecting Leydig cells as well as testosterone biosynthesis; Details provided by **Mekhoukhe *et al,*. (2019)**.

PDC has been widely recognized as a factor causing damage to testicles (**referenced from Morsy *et al.*, 2023**).

A previous study actually showed that daily oral administration of PDC for 8 weeks in rats induced oxidative stress in the testis, which was indicated by a significant increase in MDA, NO, and GSSG in the testis due to PDC consumption. In addition, significant decreases in testicular SOD, CAT, GSH, and Car levels were observed in the PDC group compared to those in the control group – all results consistent with previous reports showing how PDC-induced oxidative stress leads to testicular dysfunction (as elucidated **by Marouani *et al.*, 2017**).

The important roles of SOD, CAT and GSH in antioxidant action leading to the reduction of free radicals and ensuring tissue antioxidant balance are well documented (**Ighodaro & Akinloye, 2018**). MDA stands as a stable end product of lipid peroxidation pathways – and is widely recognized as an indirect marker showing increased intracellular ROS generation (**Cherian *et al.*, 2019**).

Ginseng protects folliculogenesis by modulating several hormone levels in the body as well as stimulating cell proliferation and reducing cellular apoptosis via antioxidant effects in the ovary: including downregulation of apoptotic markers (**Salem *et al.*, 2022**). Ginseng protects other endocrine glands, such as thyroid glands, from damage caused by PDC model mice (**Ibrahima *et al.*,2018)**.

The results of the above study show that compared with animals with benign prostatic hyperplasia, ginseng administration significantly reduces DHT levels in the prostate and supports the balance between cell proliferation and cell death, allowing the proliferation process to dominate and inhibiting apoptosis. practical (**Shin *et al.*, 2012**).

The second important finding was the positive effect of ginseng extract on PDC toxicity.

The benefits of ginseng depend on the many active ingredients found in the plant extract. Recent research shows that ginseng contains a large number of active ingredients, including ginsenosides, ginseng peptides, ginseng polysaccharides, and others. Among them, ginsenosides are important active ingredients in the physiological activity of ginseng, which have effects on the nervous system, cardiovascular system, and immune system (**Zheng *et al.*, 2018**).

Ginsenoside K compound, derived from Panax ginseng, has anti-apoptotic, anti-inflammatory and antioxidant effects. It can also protect meiotic maturation of porcine oocytes from damage caused by benzo(a)pyrene (**Luo *et***

***al* .,2020**). Another compound of ginseng is ginsenoside Rb1, which has been shown to enhance keratinocyte migration and stimulate skin wound healing (**Shin *et al.*, 2018**).

In addition, Rb3 can also improve the antioxidant capacity of diabetic mice, significantly increase the content of serum superoxide dismutase (SOD), and reduce the content of the lipid peroxidation product malondialdehyde (MDA). This is essential to reduce the risk of disease (**Ridha & Al-Shawi, 2017**).

Ginseng prevents oxidative damage, enhances the effects of antioxidants, and reduces free radicals in alloxan-treated rats (**Kim *et al.*, 2011**).Yet another ginseng compound (ginsenoside Rf) has anti-inflammatory properties against intestinal diseases due to its ability to inhibit the mitogen-activated protein kinase (MAPK)/nuclear factor kappa B (NF-κB) signaling pathway (**Ahn *et al.*, 2016**).

## 4.3 Treatment of toxicity of dichromate by Ginseng extract

**Table 4.2. Effect of treatment by ginseng extract on the biomarkers in dichromate toxified rats**

| | Group 2 | Group 5 | F | p |
|---|---|---|---|---|
| **MDA nmol/ml** | **14.52±1.12** | **12.86±2.95** | 1.370 | 0.275 |
| **SOD U/ml** | **254.77±67.46** | **254.37±66.07** | <0.001 | 0.993 |
| **Catalase U/ml** | **4.55±0.76** | **6.37±0.7** | 15.504 | 0.004 |
| **LH-Ab IU/L** | **2.88±0.67** | **3.32±0.76** | 0.965 | 0.355 |
| **DHT pg/ml** | **134.2±42.04** | **237.4±52.99** | 11.637 | 0.009 |
| **FSH ng/ml** | **15.15±2.19** | **18.04±2.74** | 3.387 | 0.103 |

**Group 2: dichromate-toxified animal group, Group 5: dichromate-toxified animals treated with ginseng extract. MDA: malondialdehyde, SOD: Superoxide dismutase, LH-Ab: Antibodies against luteinizing hormone, DHT: Dihydrotestosterone, FSH: Follicular-stimulating hormone. p-value of 0.05 was used for statistical significance,(p)= probability values and (F)= F-statistic value**

The effect of ginseng on the toxicity by PDC is studied by comparison between the group received PDC (Group 2) with the group received PDC and ginseng extract (Group 5) as presented in Table (4.2)

The serum level of SOD is increased in Group 5 compared with the Group 2. While there is a significant increase in DHT level in Group 5 compared with Group 2. Serum level of MDA, SOD, LH-Ab, and FSH between groups.

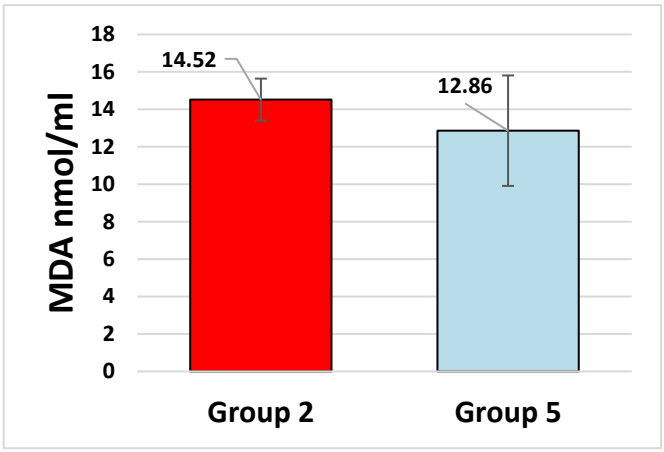



**Figure 4.13. Serum malondialdehyde (MDA) level in dichromate toxified rats' group (Group 2), and after treatment by ginseng extract (Group 5).**

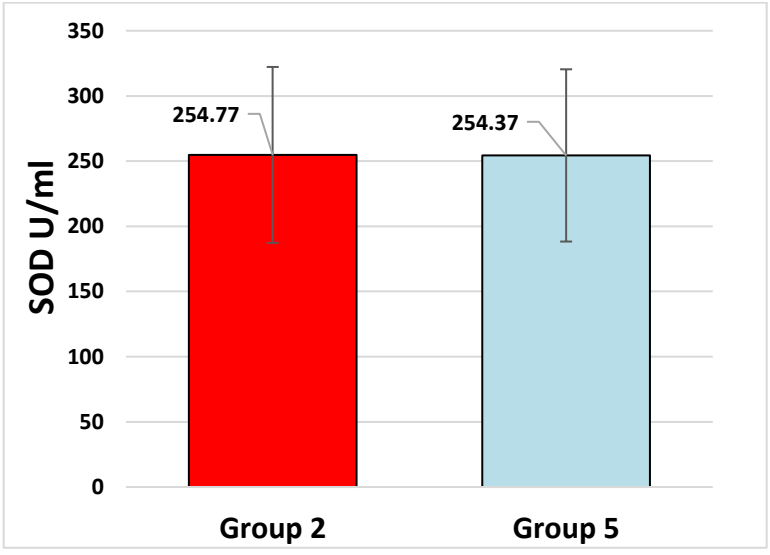



**Figure 4.14. Serum superoxide dismutase (SOD) activity in dichromate toxified rats' group (Group 2), and after treatment by ginseng extract (Group 5).**

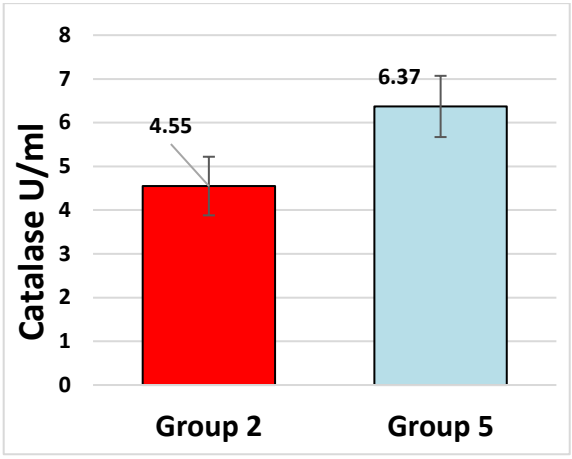



**Figure 4.15. Serum Catalase activity in dichromate toxified rats' group (Group 2), and after treatment by ginseng extract (Group 5).**

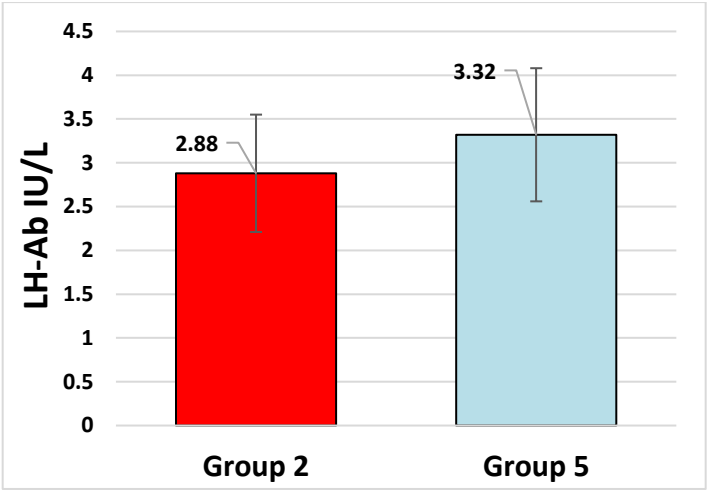



**Figure 4.16. Serum luteinizing hormone antibodies (LH-Ab) level in dichromate toxified rats' group (Group 2), and after treatment by ginseng extract (Group 5).**

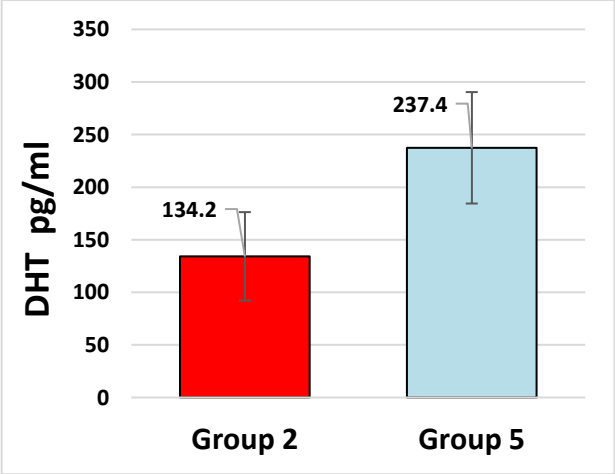



**Figure 4.17. Serum dihydrotestosterone (DHT) level in dichromate toxified rats' group (Group 2), and after treatment by ginseng extract (Group 5).**

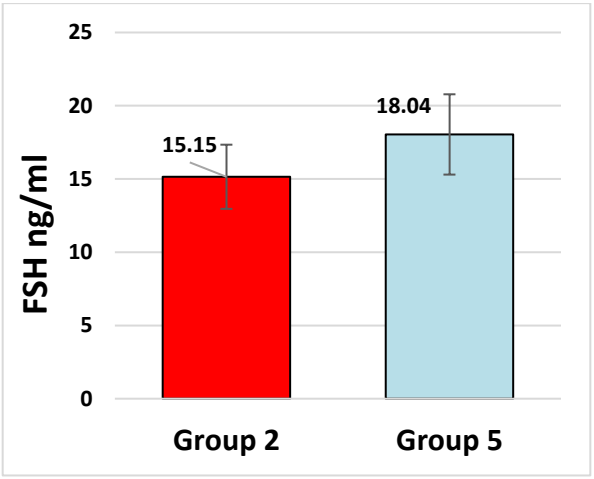



**Figure 4.18. Serum follicular-stimulating hormone (FSH) level in dichromate toxified rats' group (Group 2), and after treatment by ginseng extract (Group 5).**

The significant decrease in MDA levels and increase in SOD activity in the ginseng-treated group (group 5) supports the potential antioxidant effect of ginseng extract against PDC-induced oxidative stress. This aligns with previous research by **Rasool *et al.* (2014),** who demonstrated that exposure to PDC increases oxidative stress in male mice. The antioxidant properties of ginseng have been documented in studies such as **Ratan *et al*. (2021),** suggesting its potential role in boosting SOD activity.

The unexpected increase in DHT levels in group 5 raises questions about the effect of ginseng on sex hormones. While ginseng can have various health benefits, its effects on sex hormones are not fully understood. An increase in DHT may have adverse consequences depending on the context. More research is needed to determine whether this rise in DHT is related to ginseng's specific interaction with the hormonal system or an indirect result of its other effects. Studies like **Wang *et al*. (2023)** focused on ginseng's protective effects on male reproductive health, but the impact on DHT levels wasn't explicitly addressed .

## 4.4 Treatment of toxicity of dichromate by Ginsing-NP

**Table 4.3. Effect of treatment by 0.15ml (groups 6) and 0.3ml (groups 7) of ginseng-nanoparticles on the biomarkers in dichromate-toxified rats**

| | Group 2 [A] | Group 6 [B] | Group 7 [C] | F | Sig. |
|---|---|---|---|---|---|
| **MDA nmol/ml** | 14.52±1.12 | 11.89±5.63 | 13.28±0.76 | 0.774 | 0.483 |
| **SOD U/ml** | 254.77±67.46 [B] | 342.4±21.64 [A] | 303.6±20.67 | 5.310 | 0.022 |
| **Catalase U/ml** | 4.55±0.76 | 6.17±2.47 | 5.37±1.66 | 1.039 | 0.384 |
| **LH-Ab IU/L** | 2.88±0.67 | 3.6±0.48 | 3.25±0.78 | 1.517 | 0.259 |
| **DHT pg/ml** | 134.2±42.04 [B,C] | 313.4±25.98 [A] | 269.4±42.97 [A] | 30.503 | <0.001 |
| **FSH ng/ml** | 15.15±2.19 [B,C] | 22.08±2.6 [A] | 19.56±1.5 [A] | 13.376 | 0.001 |

**[A]: Comparison with the dichromate treated group (Group 2), [B]: Comparison with ginseng treated group (Group 6), [C]: Comparison with ginseng-nanoparticles treated group (Group 7). MDA: malondialdehyde, SOD: Superoxide dismutase, LH-Ab: Antibodies against luteinizing hormone, DHT: Dihydrotestosterone, FSH: Follicular-stimulating hormone. p-value of 0.05 was used for statistical significance, and (F)= F-statistic value**

Table (4.3) shows the effect of ginseng nanoparticles at two concentrations: 200 mg/kg (Group 6) and 100 mg/kg (Group 7) of nanoparticles solution on the toxicity of PDC compared with Group 2 who took PDC only.

The results show that ginseng-NP, at two concentrations, have no significant effect on the levels of MDA, catalase, and LH-Ab. Serum SOD level was increased after using ginseng-NPs at a concentration of 200 mg/kg. While the level of DHT and FSH are increased after adding ginseng-NPs at concentrations of 200 and 100 mg/kg.

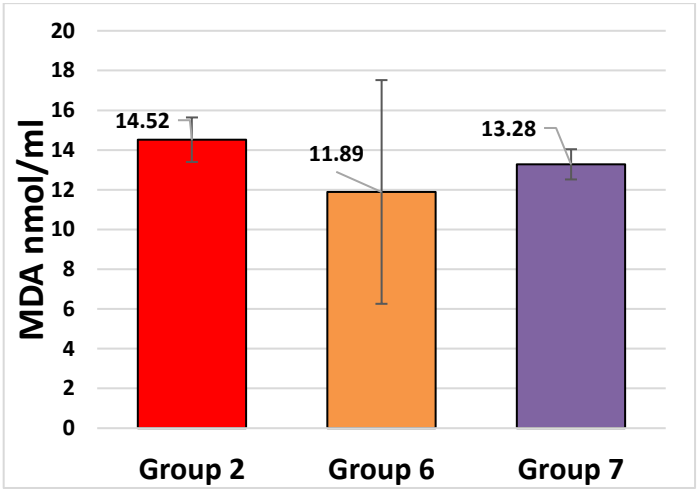



**Figure 4.19. Serum malondialdehyde (MDA) level in dichromate toxified rats' group (Group 2), and after treatment by 200 mg/kg (groups 6) and 100 mg/kg (groups 7) of ginseng-nanoparticles solution**

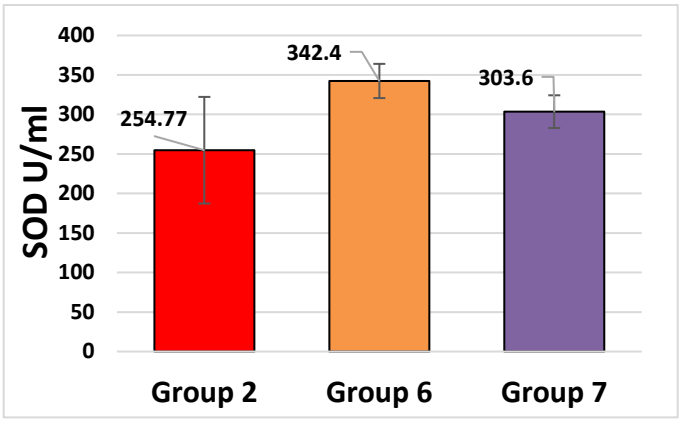



**Figure 4.20. Serum superoxide dismutase (SOD)activity in dichromate toxified rats' group (Group 2), and after treatment by 200 mg/kg (groups 6) and 100 mg/kg (groups 7) of ginseng-nanoparticles solution**

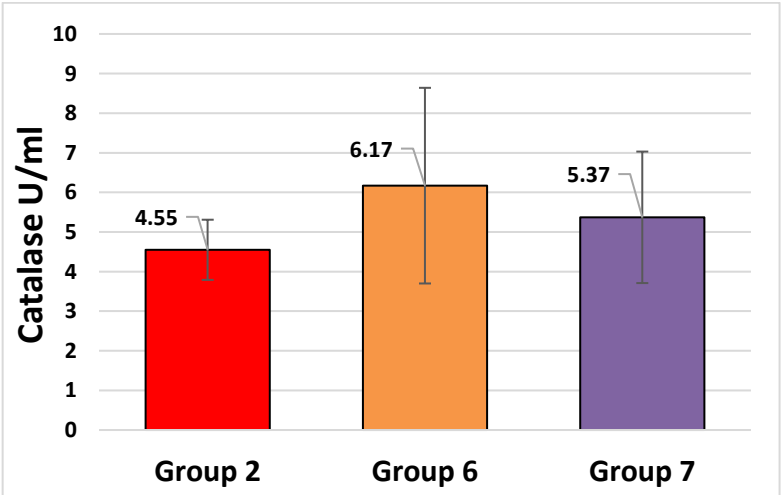



**Figure 4.21. Serum catalase activity in dichromate toxified rats' group (Group 2), and after treatment by 200 mg/kg (groups 6) and 100 mg/kg (groups 7) of ginseng-nanoparticles solution**

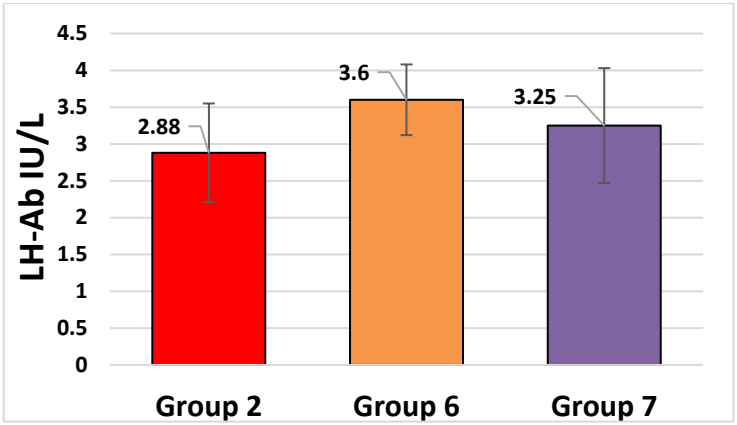



**Figure 4.22 Serum luteinizing hormone antibodies (LH-Ab) level in dichromate toxified rats' group (Group 2), and after treatment by 200 mg/kg(groups 6) and 100 mg/kg (groups 7) of ginseng-nanoparticles solution**

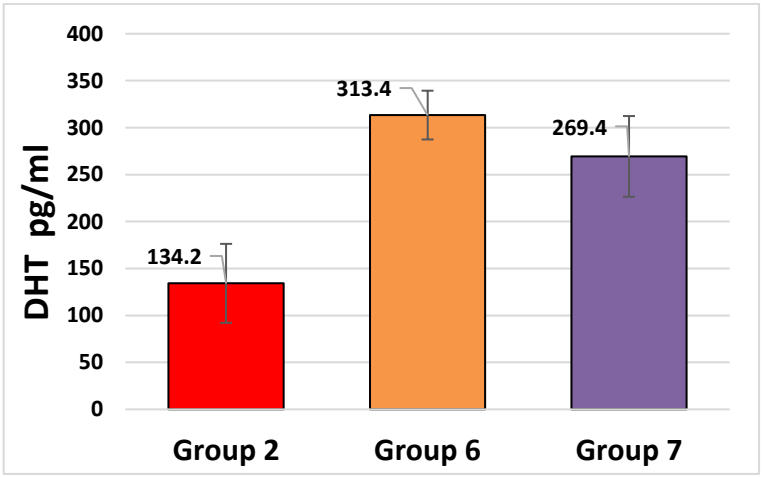



**Figure 4.23. Serum luteinizing hormone antibodies (LH-Ab) level in dichromate toxified rats' group (Group 2), and after treatment by 200 mg/kg (groups 6) and 100 mg/kg (groups 7) of ginseng-nanoparticles solution**

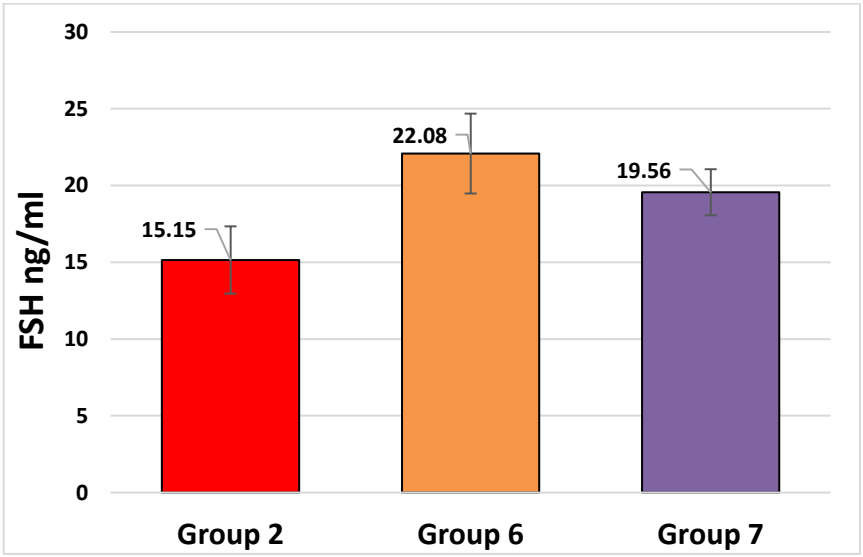



**Figure 4.24. Serum follicular-stimulating hormone (FSH) level in dichromate toxified rats' group (Group 2), and after treatment by 200 mg/kg (groups 6) and 100 mg/kg (groups 7) of ginseng-nanoparticles solution**

The other important finding is the antitoxic activity of ginseng-NP in the treatment of PDC toxicity as presented in Table (4.3). This effect is directly proportional to the concentration of ginseng-NPs. NPs are small—nano-sized, less than 100 nm—yet they exhibit an exceptionally broad and expansive range of physical and chemical properties. These NPs possess distinct features due to their high surface energy—a high fraction of surface atoms, reduced defects, and spatial confinement make them unique nanostructures. Due to its small size and excellent physical and chemical properties, nanotechnology can find applications in various branches of biomedicine (**Gomaji Chaudhary *et al.*, 2015**).

In last years, NPs have emerged as highly promising tools widely used for applications in biomedicine (McNamara & Tofail, 2017). NPs combine biology, chemistry, physics as well as materials science leading to the development of new therapeutic materials based on nano-sized materials that will be used in various biomedical applications. Thanks to their small size allowing easy entry into cells - and thus being able on their own to serve purposes in biomedicine: antioxidants without even being loaded onto any other carrier systems - NPs can also act as anti-inflammatory agents or as diagnostics through imaging (Farhan et al., 2023) with drug carriers or bioconjugates delivered using biological therapies since they are also effective transport systems themselves.

Furthermore, they are commonly used with drug compounds that deliver bioconjugates to target sites for use in therapy. When hexavalent chromium is converted into trivalent chromium inside cells, ROS is said to be formed **(Stohs *et al.*, 2001**). The cause of vasoconstriction may be due to lipid oxidation as reported by (**El-Sakhawy *et al.*, 2017**).

Potassium dichromate causes an increase in intracellular levels of nitric oxide (NO), which activates nuclear factor kappa B (NF-KB), “a critical activator of genes involved in inflammation, immunity, and apoptosis,” leading

to an increase in apoptosis, through ROS-induced DNA damage and its activation of p53 **(Kawanishi *et al.*, 2002**).

Ginseng reduced biomarkers of oxidative stress in this study by reducing oxidative stress biomarkers, as seen by **Sun *et al* ,Jadhav & Saudagar, 2014)**.

## 4.5 Histopathologic results.

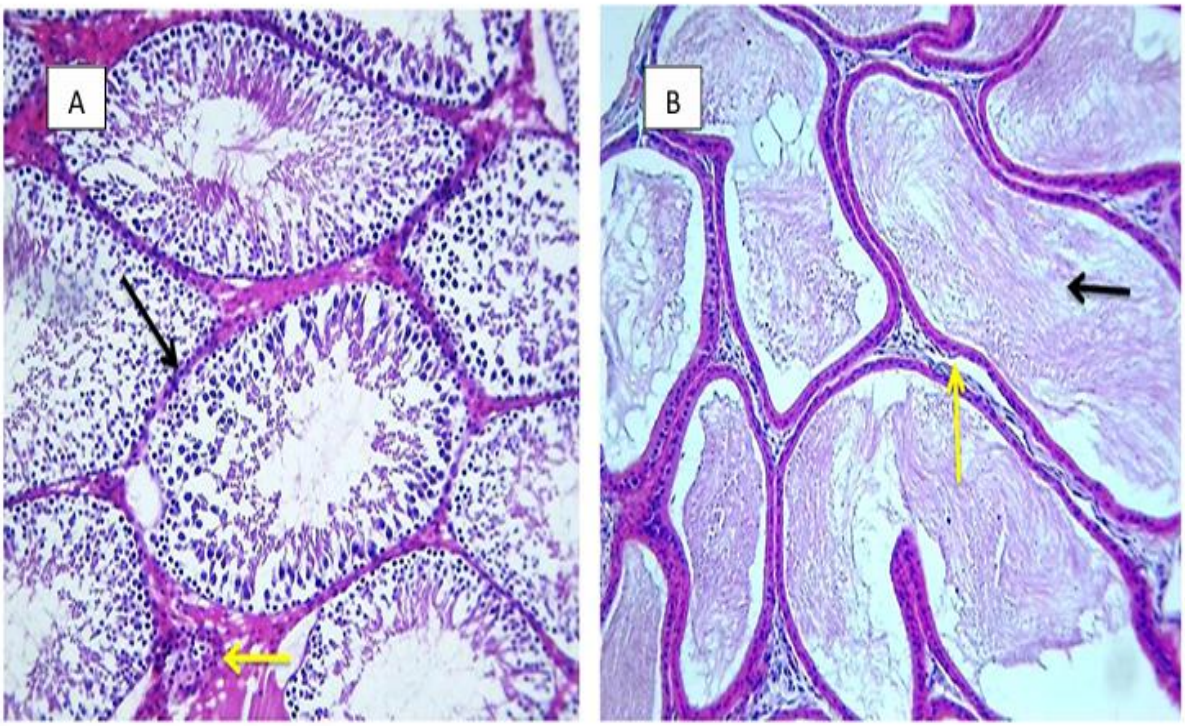



**Figure ( 4. 25 ) A: Microscopical examination of a control rat testes showing the normal histological architecture of testicular structure, normal rounded to oval shaping of seminiferous tubules (black arrow) , obvious and normal surrounding Leydig cells (yellow arrow).(H and E, 10X). B: Histological examination of a control rat epididymis showing the normal histological structure of epididymal tubules (yellow arrow), normal spermatic density (black arrow) .(H and E, 10X).**

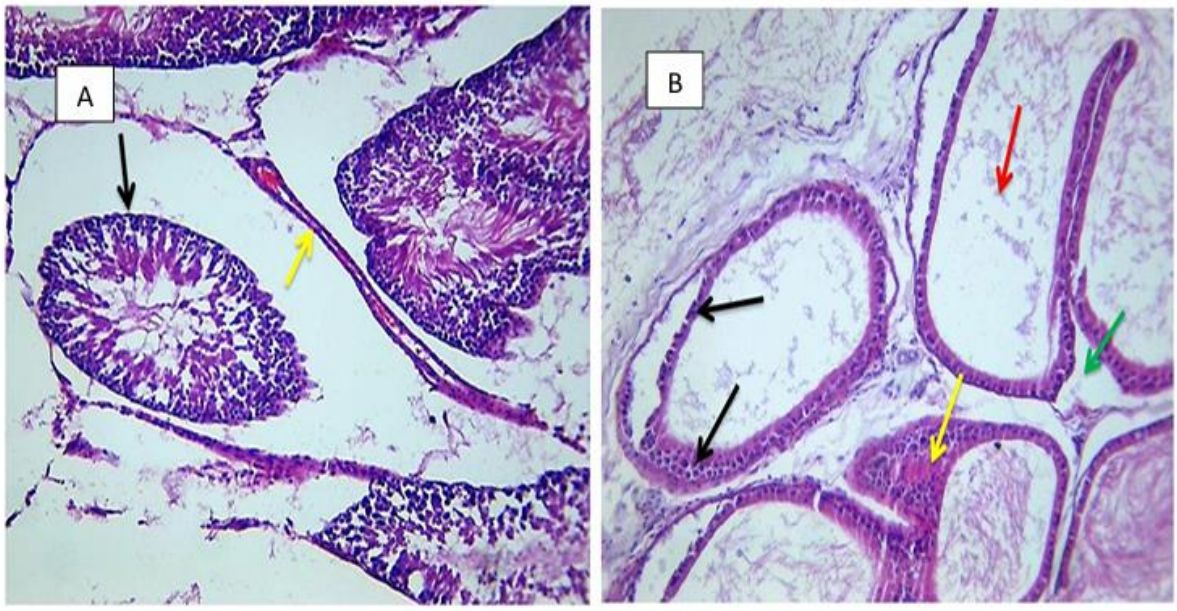



**Figure (4. 26 ) A: Microscopical examination of testicular tissue section of Potassium Dichromate treated animal showing significant histological alterations of seminiferous tubules structure, manifested by atrophy of tubules (black arrow) , marked congestion of interstitial blood vessles (yellow arrow).(H and E, 10X). B: Microscopical examination of epididymis of Potassium Dichromate treated animal showing significant changes in tubular epithelia, marked hyperplasia in tubular epithelia with sloughing (black arrow), hyaline deposition (yellow arrow), low spermatic density (red arrow) , with widening in interstitial spaces (green arrow).(H and E, 10X).**

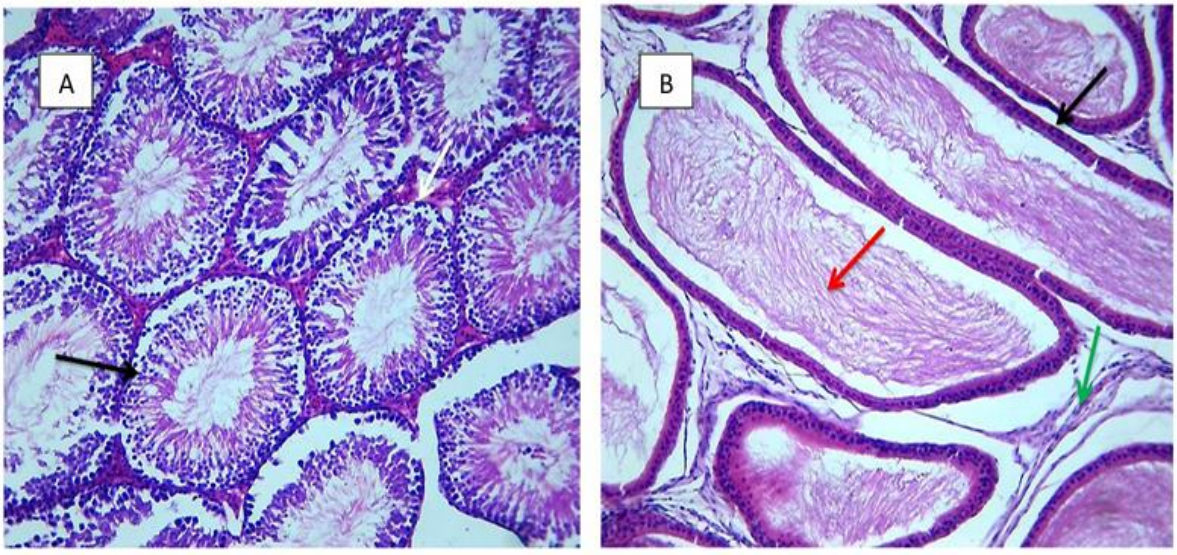



**Figure (4. 27) A: Microscopical examination of testes for Ginseng extract treated animal revealing the normal testicular tissue structure (black arrow), remarkable interstitial tissue blood vesseles congestion (white arrow).(H and E, 10X).B: Microscopical examination of epididymis of Ginseng extract treated rat revealing normal epididymal tubules, with some elongation (black arrow), decent spermatic density (red arrow) , with widening in interstitial spaces (green arrow).(H and E, 10X).**

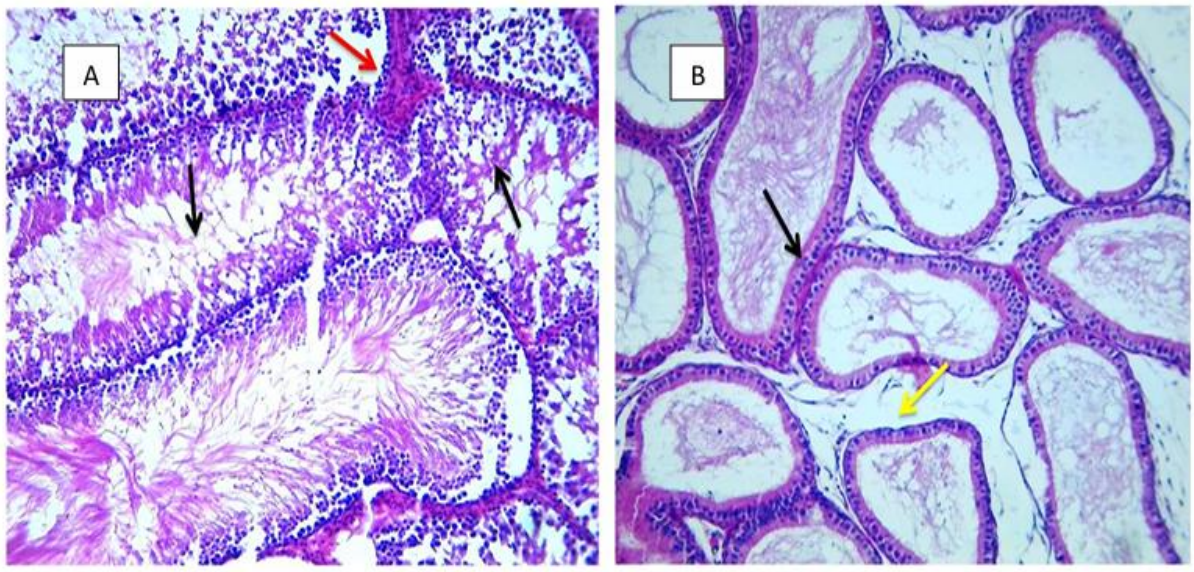



**Figure (4.28) A: histological examination of testicular tissue section of Ginseng Nanoparticles treated rat revealing to a certain extent slight or mild alterations of some seminiferous tubules structure, represented by some degeneration in germinal epithelium (black arrow) , marked congestion of interstitial blood vessles (yellow arrow).(H and E, 10X).B: histological examination of epididymis section of Ginseng Nanoparticles treated rat revealing moderately alterations of some epididymal tubules structure, represented by degeneration in germinal epithelium (black arrow) , marked dilation in interstitial spaces(yellow arrow).(H and E, 10X).**

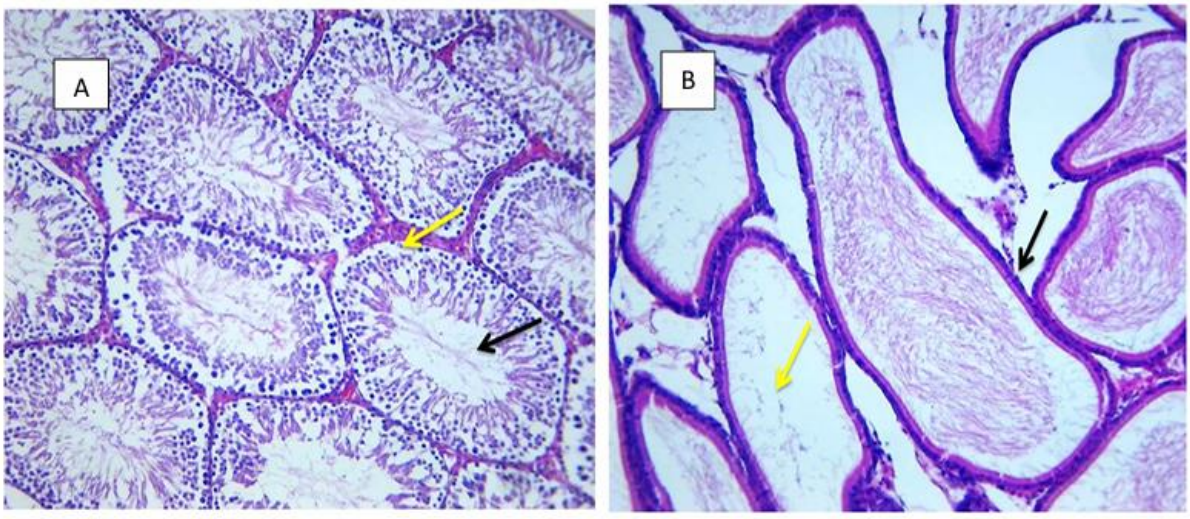



**Figure (4. 29 ) A: Microscopical examination of testes of Potassium Dichromate and Ginseng extract treated rat revealing significant improvements of seminiferous tubules morphology, normal germinal epithelium with slight degeneration in some tubules(black arrow) , marked congestion of interstitial blood vessles (yellow arrow).(H and E, 10X). B: Microscopically examination of epididymis section of Potassium Dichromate and Ginseng extract treated rat revealing normal tubule morphology (black arrow) , with mild to moderate sperm population (yellow arrow).(H and E, 10X).**

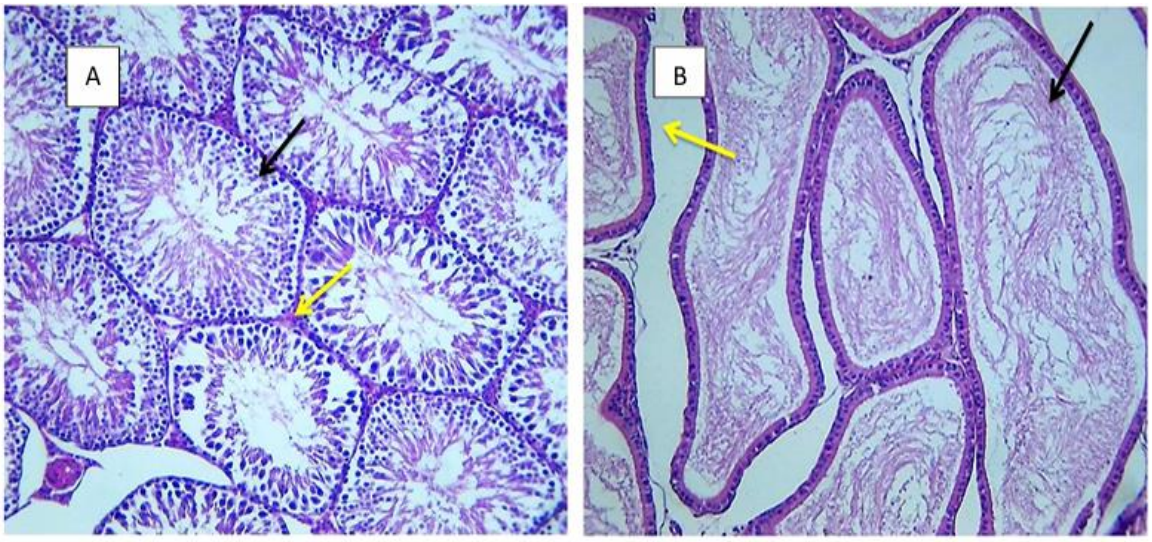



**Figure (4.30 ) A: histological examination of testes of Potassium Dichromate and Ginseng nanoparticles 0.3 treated rat showing significant improvements and reversible changes of seminiferous tubules morphology, looks normal (black arrow) , normal interstitial spaces and Leydig cells (yellow arrow).(H and E, 10X).B: histological examination of epididymis of Potassium Dichromate and Ginseng nanoparticles 0.3 treated rat showing significant improvements in tubules morphology, normal spermatic population (black arrow) , normal interstitial spaces with slight dilation(yellow arrow).(H and E, 10X).**

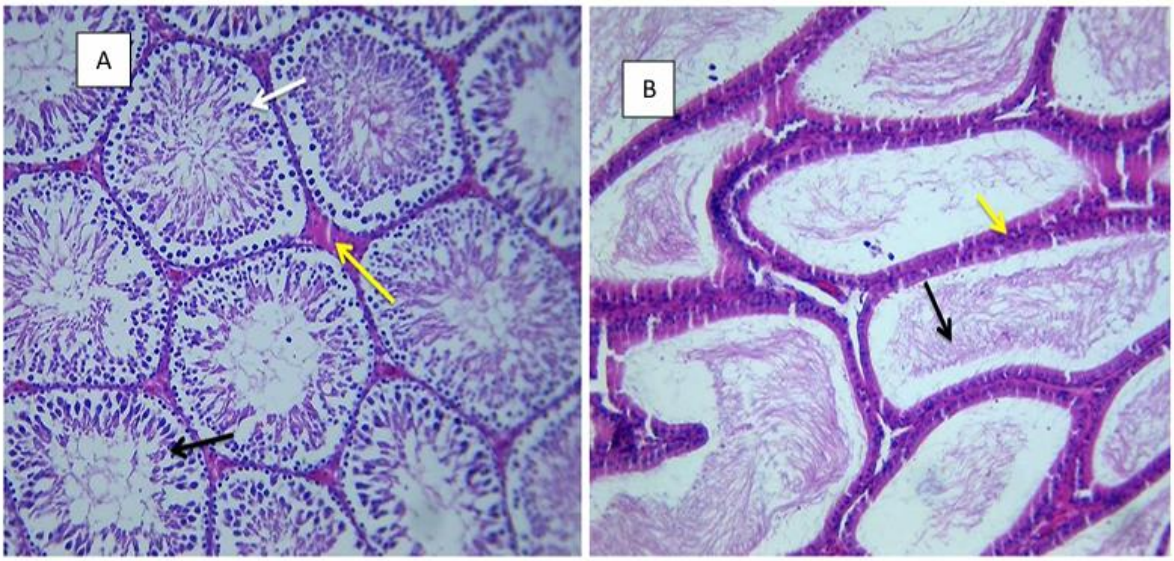



**Figure (4. 31) A: histological examination of testes of Potassium Dichromate and Ginseng nanoparticles 0.15 treated rat showing semi normal structure of testicular tissue (black arrow) some tubules undergoes sloughing(white arrow), congested interstitial tissue spaces (yellow arrow).(H and E, 10X). B: histological examination of epididymis of Potassium Dichromate and Ginseng nanoparticles 0.15 treated rat showing significant alterations manifested by, moderate to normal spermatic population (black arrow) , disarrangements in tubular epithelia(yellow arrow).(H and E, 10X)**

Microscopic examination of control rat testes and epididymis as shown in Figure (4.25) displaying normal histological features provides valuable insights into the basic properties of healthy testicular tissue. This observation underscores the importance of maintaining the structural integrity of seminiferous tubules and Leydig cells for proper testicular function and spermatogenesis, as supported by previous studies **(Adamczewska *et al.*, 2022)**.which emphasized the importance of these normal histological features in male reproductive health.

Microscopic examination of testicular and epididymal tissue sections from potassium dichromate-treated animals as seen in Figure (4.26) revealed significant histopathological changes indicative of testicular and epididymal toxicity. Observed changes include tubular atrophy, empty tubules, congestion of interstitial blood vessels, degeneration of the germinal epithelium, areas of epithelial necrosis, changes in the tubular epithelium, degeneration of spermatids, developmental nuclei, decreased sperm density, and widening of interstitial spaces. The implication of these findings is that male reproductive tissues may have been seriously damaged as a result of potassium dichromate. There have been previous investigations into the effects of hexavalent chromium, including potassium dichromate, on testicular function and ultimately male reproductive health. It has been proven through research that exposure to chromium compounds can not only induce changes in spermatogenesis and lead to testicular dysfunction, but also lead to histological modifications in the testicular and epididymal tissues (**Dong *et al*.,2021**).

Oxidative stress has thus found itself in pole position among other aspirants like mitochondrial damage plus disruption of normal testicular physiology as likely pathophysiologic mechanisms contributing towards chromium-induced testicular toxicity. The findings, therefore, corroborate what

previous researchers had noted about histopathological changes in the testicular and epididymal tissues due to Potassium Dichromate treatment: that they paint grim pictures for male reproductive health because of chromium exposure **(Bashandy *et al*.,2021**).

In conclusion, they call for further studies aimed at unraveling these mechanisms as well as possible therapeutic interventions because understanding them will help reduce this growing concern about the harmful effects of such exposure on males - especially their reproductive abilities **(Marouani *et al.*, 2012).**

Figure (4.27) showed positive effects on testicular and epididymal tissues in animals treated with ginseng extract. A normal structure of testicular tissue with marked congestion of the blood vessels of the interstitial tissues of the testes was observed at 10X magnification. The seminiferous tubules appeared normal with widened interstitial spaces and normal spermatogenesis, indicating the positive effect of ginseng extract treatment on testicular health and spermatogenesis.

Normal epididymal tubules with some elongation were observed at 10X magnification in the epididymis, along with decent sperm density and widened interstitial spaces.The epididymal tubules appeared normal with adequate sperm density and wide interstitial spaces – meaning that treatment with ginseng extract may help maintain normal epididymal structure and sperm quality. Previous scientific studies supporting the benefits of ginseng extract on testicular and epididymal health provide scientific evidence consistent with the observed histological improvements in animal testicles and epididymis visualized through microscopic examinations resulting from ginseng treatment (**Jang *et al.*, 2011**).

Examination of testicular and epididymal tissue sections revealed changes in their structure as shown in Figure (4.28). Testicular tissue showed slight degeneration at 10X magnification, along with marked congestion of the interstitial blood vessels, whereas observations included mild disruption of the germinal tubular epithelium and Leydig cell degeneration. In the epididymis, the changes observed at 10X magnification were somewhat different, some showing degeneration of the germinal epithelium as well as marked dilation of the interstitial spaces; These changes led to the development of a hyperplastic cellular epithelium and moderate sperm density was noted. Previous scientific research studies have highlighted the impact of ginseng and its derivatives on male reproductive health: specifically those insights coming from the effects seen directly within the testicular as well as epididymal tissue **(El-belbasy *et al*.,2021)**

Previous investigations generally indicate that ginseng and its cousins can achieve good things in the world of the testicle and epididymis. The changes observed during histological examination of testicular and epididymal tissue after ginseng nanoparticle treatment may be like looking into a fog – a mysterious dance between the vital elements of ginseng and reproductive tissue. It calls for more scientific research to shed light on the mysterious mechanisms at play **(Emran *et al*.,2021; Alnabi *et al*.,2022)**

The morphological changes observed in the seminiferous tubules and epididymis of mice treated with a mixture of potassium dichromate and ginseng extract under a light microscope are as shown in Figure (4.29). They include normal germinal epithelium with slight degeneration of some tubules, and marked interstitial vascular congestion at both ends of before them. Others presented a quite distinct case. The presence of normal sperm was noted alongside the normal sperm cells that were only found as there was no indication of future development of these cells due to their location between two areas

showing crowding. This information served as a point of reference towards the ongoing spermatogenesis process within the tissue sections examined, although it was noted that some sections did not support this activity.

These details highlight possible protective effects that Ginseng extract might have on testicular and epididymal tissues even when co-administered with Potassium Dichromate. An established toxicant, such positive outcomes resulting from concomitant administration (despite adverse effects associated with individual agents) could provide more insight into potentials for ginseng's protective action on male reproductive system: Given findings from previous research works demonstrating its capability to prevent against reproductive toxicity and enhance spermatogenesis. For example, One study showed that ginseng extract protected mice from dexamethasone-induced reproductive toxicity **(Aziz *et al*.,2024)**,while another study indicated that it improved spermatogenesis even in mice with testicular damage caused by heat stress **( Cai *et al*.,2021)**

Histological analysis of rat testes and epididymis after treatment with potassium dichromate and 0.3 ginseng nanoparticles (shown in Figure (4.30) showed marked improvements as well as reversible changes in tissue morphology. At 10X magnification, the seminiferous tubules showed a typical architecture characterized by normal interstitial spaces and Leydig cells while at 40X magnification, the germinal epithelium appeared intact with sperm, spermatocytes, and normal spermatids.

The results in the epididymis also showed improvements – at 10X magnification the shape of the tubules was close to normal with a healthy sperm count and the spaces were slightly dilated. Observations made that the epididymal tubules were indeed normal with an adequate number of sperm and an orderly arrangement of the tubular epithelium. These collective results indicate a positive effect of the combination of potassium dichromate and

ginseng nanoparticles 0.3 on testicular as well as epididymal health – an effect that promotes growth by enhancing tissue morphology and thus spermatogenesis.

The literature has previously highlighted the preventive and therapeutic effects of ginseng on testicular health including protection from toxicants that cause testicular atrophy such as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), confirming our findings. Furthermore, studies have demonstrated a protective role of ginseng against oxidative injury in rat testicular tissue injury, thus supporting the improvements observed among those treated with D-galactose as well as ginseng nanoparticles 0.3(**Erthal *et al.*, 2018**).

Histological examination reveals the testicular structure of 0.15 potassium dichromate and ginseng nanoparticles treated rat (see Figure (4.31) showing some elements of tubular dissection within an almost normal crowded interstitial space. The findings from the seminiferous tubules indicate degeneration of the germinal epithelium and sperm necrosis, while those from the epididymis show significant changes with moderate to normal populations with sperm disorders as well as the distribution of epithelial cells along the tubules.

These observations indicate that potassium dichromate with ginseng nanoparticles 0.15 has a moderate protective effect on testicular and epididymal health leading to improvements in tissue morphology and indices of spermatogenesis. Studies have previously demonstrated the preventive and therapeutic effects of ginseng on testicular health including protection against atrophy caused by TCDD; This study will therefore evaluate the ameliorative effects of WA on DM-induced male reproductive dysfunction in rats based on these positive results. The results indicated that WA treatment led to improved sperm count and motility among diabetic rats suggesting potential protective roles towards testicular components especially when considered alongside other relevant findings related to the alterations seen after use of potassium

dichromate to aspect of ginseng nanoparticles 0.15 indicating efficacy through protection against damage from toxic substances: supportive literature indicates high potential for ginseng as well (**Al-saadi, 2017**).

# Chapter Five
# Conclusions and Recommendations

# 5. Conclusions & Recommendations

## 5.1 Conclusions

1. The results showed that exposure to potassium dichromate led to decreased levels of testosterone and decreased levels of FSH and LH hormones in the blood serum.

2. Higher levels of the oxidative stress indicator MDA and lower levels of antioxidants SOD and catalase were also observed in blood serum in the group exposed to potassium dichromate.

3. Histological study of the testicle showed pathological changes in the group exposed to potassium dichromate compared to the control group.

4. The groups that received ginseng or nano-ginseng showed improvements in hormone levels and antioxidant indicators compared to the potassium dichromate group, indicating the ability of ginseng to mitigate the toxic effects of potassium dichromate on the male reproductive system.

## 5.2 Recommendations

1. It is recommended to avoid exposure to potassium dichromate as much as possible due to its toxic effects on the male reproductive system.

2. Ginseng or nano-ginseng can be used as a complementary treatment to mitigate the toxic effects of potassium dichromate on testicular and reproductive functions.

3. More in-depth studies are recommended to determine the precise mechanisms by which ginseng mitigates these toxic effects.

4. More research should be done to evaluate the long-term effects of potassium dichromate and ginseng on reproductive health.

5. More research should be done to evaluate the effects of ginseng on Cancer diseases.

# Chapter Six

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# APPENDIXES

## Appendix(1):Estimation of Testosterone Hormone (T) Concentration (ng/ml).

## Principle:

This ELISA kit uses Sandwich-ELISA as the method. The Microelisa stripplate provided in this kit has been pre-coated with an antibody specific to DHT. Standards or samples are added to the appropriate Microelisa stripplate wells and combined to the specific antibody. Then a Horseradish Peroxidase (HRP)- conjugated antibody specific for DHT is added to each Microelisa stripplate well and incubated. Free components are washed away. The TMB

substrate solution is added to each well. Only those wells that contain DHT and HRP conjugated DHT antibody will appear blue in color and then turn yellow after the addition of the stop solution. The optical density (OD) is measured spectrophotometrically at a wavelength of 450 nm. The OD value is proportional to the concentration of DHT. You can calculate the concentration of DHT in the samples by comparing the OD of the samples to the standard curve.

## Sample preparation .

### Serum preparation.

After collection of the whole blood, allow the blood to clot by leaving it undisturbed at room temperature. This usually takes 10-20 minutes. Remove the clot by centrifuging at 2000 - 3000 rpm for 20 minutes. If precipitates appear during reservation, the sample should be centrifugated again.

**The test procedure was conducted in accordance with the following steps:**

1. Dilution of Standards Ten wells are set for standards in a Microelisa stripplate. In Well 1 and Well 2, 100µl Standard solution and 50µl Standard Dilution buffer are added and mixed well. In Well 3 and Well 4, 100µl solution from Well 1 and Well 2 are added respectively. Then 50µl Standard Dilution buffer are added and mixed well. 50µl solution is discarded from Well 3 and Well 4. In Well 5 and Well 6, 50µl solution from Well 3 and Well 4 are added respectively. Then 50µl Standard Dilution buffer are added and mixed well. In Well 7 and ell 8, 50µl solution from Well 5 and Well 6 are added respectively. Then 50µl Standard Dilution buffer are added and mixed well. In Well 9 and Well 10, 50µl solution from Well 8 are added respectively. Then 50µl Standard Dilution buffer are added and mixed well. 50µl solution is discarded from

Well 9 and Well 10. After dilution, the total volume in all the wells are 50µl and the concentrations are 480 pg/ml, 320 pg/ml,160 pg/ml, 80 pg/ml and 40 pg/ml, respectively

2. In the Microelisa stripplate, leave a well empty as blank control. In sample wells, 40µl Sample dilution buffer and 10µl sample are added (dilution factor is 5). Samples should be loaded onto the bottom without touching the well wall. Mix well with gentle shaking.
3. Incubation: incubate 30 min at 37℃ after sealed with Closure plate membrane.
4. Dilution: dilute the concentrated washing buffer with distilled water (30 times for 96T and 20 times for 48T).
5. ashing: carefully peel off Closure plate membrane, aspirate and refill with the wash solution. Discard the wash solution after resting for 30 seconds. Repeat the washing procedure for 5 times.
6. Add 50 µl HRP-Conjugate reagent to each well except the blank control well.
7. Incubation as described in Step 3.
8. ashing as described in Step 5.
9. Coloring: Add 50 µl Chromogen Solution A and 50 µl Chromogen Solution B to each well, mix with gently shaking and incubate at 37℃ for 15 minutes. Please avoid light during coloring.
10. Termination: add 50 µl stop solution to each well to terminate the reaction. The color in the well should change from blue to yellow.
11. Read absorbance O.D. at 450nm using a Microtiter Plate Reader. The OD value of the blank control well is set as zero. Assay should be carried out within 15 minutes after adding stop solution.

**Precision .**

Intra-assay Precision (Precision within an assay): 3 samples with low, middle and high level Rat DHT were tested 20 times on one plate, respectively. Inter-assay Precision (Precision between assays): 3 samples with low, middle and high level Rat DHT were tested on 3 different plates, 8 replicates in each plate.

CV(%) = SD/meanX100

Intra-Assay: CV<10%

Inter-Assay: CV<12%.

## appendix (II): Estimation Follicular Stimulating Hormone (FSH) Concentration (mlU/ml).

**Principle.**

This ELISA kit uses Sandwich-ELISA as the method. The Microelisa stripplate provided in this kit has been pre-coated with an antibody specific to FSH Standards or samples are added to the appropriate Microelisa stripplate wells and combined to the specific antibody. Then a Horseradish Peroxidase (HRP)-conjugated antibody specific for FSH is added to each Microelisa stripplate well and incubated. Free components are washed away. The TMB substrate solution is added to each well. Only those wells that contain FSH and HRP conjugated FSH antibody will appear blue in color and then turn yellow after the addition of the stop solution. The optical density (OD) is measured spectrophotometrically at a wavelength of 450 nm. The OD value is proportional to the concentration of FSH You can calculate the concentration of FSH in the samples by comparing the OD of the samples to the standard curve.

# Sample preparation .

## Serum preparation.

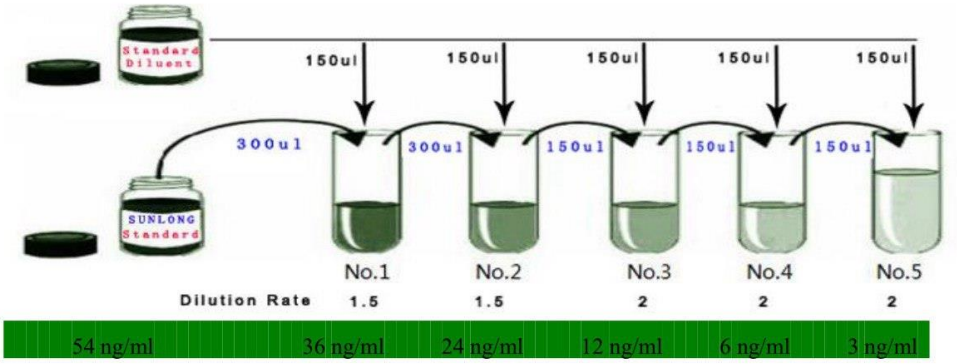
After collection of the whole blood, allow the blood to clot by leaving it undisturbed at room temperature. This usually takes 10-20 minutes. Remove the clot by centrifuging at 2000 – 3000 rpm for 20 minutes. If precipitates appear during reservation, the sample should be centrifugated again.

## Procedure.

1. Dilution of Standards

   Dilute the standard by small tubes first, then pipette the volume of 50ul from each tube to microplate well,each tube use two wells, total ten wells.

| | | |
|---|---|---|
| 36 ng/ml | Standard No.1 | 300µl Original Standard + 150µl Standard diluents |
| 24 ng/ml | Standard No.2 | 300µl Standard No.1 + 150µl Standard diluents |
| 12 ng/ml | Standard No.3 | 150µl Standard No.2 + 150µl Standard diluent |
| 6 ng/ml | Standard No.4 | 150µl Standard No.3 + 150µl Standard diluent |
| 3 ng/ml | Standard No.5 | 150µl Standard No.4 + 150µl Standard diluent |




2. In the Microelisa stripplate, leave a well empty as blank control. In sample wells, 40µl Sample dilution buffer and 10µl sample are added (dilution factor is 5). Samples should be loaded onto the bottom without touching the well wall. Mix well with gentle shaking.
3. Incubation: incubate 30 min at 37℃ after sealed with Closure plate membrane.

4. Dilution: dilute the concentrated washing buffer with distilled water (30 times for 96T and20 times for 48T).
5. Washing: carefully peel off Closure plate membrane, aspirate and refill with the wash solution. Discard the wash solution after resting for 30 seconds. Repeat the washing procedure for 5 times.
6. Add 50 µl HRP-Conjugate reagent to each well except the blank control well.
7. Incubation as described in Step 3.
8. Washing as described in Step 5.
9. Coloring: Add 50 µl Chromogen Solution A and 50 µl Chromogen Solution B to each well, mix with gently shaking and incubate at 37 ℃ for 15 minutes. Please avoid light during coloring.
10. Termination: add 50 µl stop solution to each well to terminate the reaction. The color in the well should change from blue to yellow.
11. Read absorbance O.D. at 450nm using a Microtiter Plate Reader. The OD value of the blank control well is set as zero. Assay should be carried out within 15 minutes afteradding stop solution.

**Precision .**

Intra-assay Precision (Precision within an assay): 3 samples with low, middle and high level Rat DHT were tested 20 times on one plate, respectively. Inter-assay Precision (Precision between assays): 3 samples with low, middle and high level Rat DHT were tested on 3 different plates, 8 replicates in each plate.

CV(%) = SD/meanX100

Intra-Assay: CV<10%

Inter-Assay: CV<12%.

## appendix (III): Estimation of Luteinizing Hormone (LH) Concentration (ng/ml).

**Principle.**

This ELISA kit uses Sandwich-ELISA as the method. The Microelisa stripplate provided in this kit has been pre-coated with an antigen specific to LH-Ab. Standards or samples are added to the appropriate Microelisa stripplate wells and combined to the specific antigen. Then a Horseradish Peroxidase (HRP)-conjugated antigen specific for LH-Ab is added to each Microelisa stripplate well and incubated. Free components are washed away. The TMB substrate solution is added to each well. Only those wells that contain LH-Ab and HRP conjugated LH antigen will appear blue in color and then turn yellow after the addition of the stop solution. The optical density (OD) is measured spectrophotometrically at a wavelength of 450 nm. The OD value is proportional to the concentration of LH-Ab. You can calculate the concentration of LH-Ab in the samples by comparing the OD of the samples to the standard curve.

## Sample preparation .

### Serum preparation.

After collection of the whole blood, allow the blood to clot by leaving it undisturbed at room temperature. This usually takes 10-20 minutes. Remove the clot by centrifuging at 2000 - 3000 rpm for 20 minutes. If precipitates appear during reservation, the sample should be centrifugated again.

### Procedure.

1. Dilution of Standards

   Dilute the standard by small tubes first,then pipette the volume of 50ul from each tube to microplate well,each tube use two wells ,total ten wells.
2. In the Microelisa stripplate, leave a well empty as blank control. In sample wells, 40µl Sample dilution buffer and 10µl sample are added (dilution factor is 5). Samples should be loaded onto the bottom without touching the well wall. Mix well with gentle shaking.

3. Incubation: incubate 30 min at 37℃ after sealed with Closure plate membrane.
4. Dilution: dilute the concentrated washing buffer with distilled water (30 times for 96T and
   20 times for 48T).
5. Washing: carefully peel off Closure plate membrane, aspirate and refill with the wash
   solution. Discard the wash solution after resting for 30 seconds. Repeat the washing procedure for 5 times.
6. Add 50 μl HRP-Conjugate reagent to each well except the blank control well.
7. Incubation as described in Step 3.
8. Washing as described in Step 5.
9. Coloring: Add 50 μl Chromogen Solution A and 50 μl Chromogen Solution B to each well, mix with gently shaking and incubate at 37 ℃ for 15 minutes. Please avoid light during coloring.
10. Termination: add 50 μl stop solution to each well to terminate the reaction. The color in the well should change from blue to yellow.
11. Read absorbance O.D. at 450nm using a Microtiter Plate Reader. The OD value of the blank control well is set as zero. Assay should be carried out within 15 minutes after adding stop solution.

**Precision .**

Intra-assay Precision (Precision within an assay): 3 samples with low, middle and high level Rat DHT were tested 20 times on one plate, respectively. Inter-assay Precision (Precision between assays): 3 samples with low, middle and high level Rat DHT were tested on 3 different plates, 8 replicates in each plate.

CV(%) = SD/meanX100

Intra-Assay: CV<10%

Inter-Assay: CV<12%.

## appendix (IV): Serum Malondialdehyde Measurement (MDA).

Malondialdehyde was estimated by Thiobarbituric acid (TBA) assay method of Buege & Aust, (1978) on spectrophotometer

### Principle:

This method quantifies lipid peroxides by measuring aldehyde breakdown products of lipid peroxidation. Basic principle of the method is the reaction of one molecule of malondialdehyde and two molecules of Thiobarbituric acid to form a red MDA-TBA complex which can be measure at 535 nm.

Stock TCA – TBA – HCl

### Reagent:

It was prepared by dissolving 15% W/V trichloroacetic acid and 0.375% W/V Thiobarbituric acid and 0.25N HCl to make 100 ml (2.1 ml of concentrated HCl in 100 ml). This solution was mildly heated to assist in the dissolution of TBA. Dissolved 15 gm TCA and 0.375 mg Thiobarbituric acid in 0.25 N HCl and volume was made up to 100 ml with 0.25 N HCl.

### Procedure:

To 0.4 ml of serum, 0.6 ml TCA-TBA-HCl reagents were added. It was mixed well and kept in boiling water bath for 10 minutes. After cooling 1.0 ml freshly prepared 1N NaOH solution was added to eliminate centrifugation. This absorbance of pink colour was measured at 535 nm against blank which contained distilled water in place of serum. In blank 0.4 ml distilled water and 0.6 ml TCA-TBA-HCl reagent was mixed and boiled. Blank was always taken.

### Calculation:

Extinction coefficient of MDA at 535 nm is = 1.56 × 105

MDA concentration = χ / 0.0624 nmol / ml.

# Appendix (V) : Superoxide Dismutase (SOD) Activity.

## Preparation

1. Tris buffer (pH 8.0): was prepared by dissolving 0.258 gm of tris and 0.111 gm of Ethylene diamine tetra acetic acid (EDTA) in dH2O and completing the volume to 100 ml.

2. Pyragallol solution (0.2 mM): was prepared by dissolving 0.0252 gm of pyragallol with 10 ml of HCl and completing the volume to 100 ml with dH2O.

## Procedure

According to Marklund and Marklund, (1974), reaction mix is consisting of 50 µl crude enzyme extract with 2 ml of tris buffer and 0.5 ml of pyragallol (0.2 mM) which absorbs light at 420 nm. Control solution contains the same materials except for the enzyme extract that was replaced by dH2O. As a blank, dH2O was used. Single unit of enzyme is defined as the amount of enzyme that is capable of inhibiting 50% of pyragallol oxidation. SOD activity was calculated using the following equation (Ma *et al.*, 2009):

SOD activity (u/ml) = (Vp-Vs)/(Vp*0.5) *(Vt/Vs) *n

Vp=Auto oxidation rate of pyrogallol rate of pyrogallol (control)

Vs= Auto oxidation rate of sample (with enzyme)

Vt=Total reaction volume (ml)

Vs= volume of enzyme used for the assay (ml)

n= dilution fold of the SOD sample

0.5= factor for 50% inhibition

# Appendix (VI) : Determination of Serum Concentration of Catalase (CAT)

## Procedure:

Catalase activity was assessed by incubating the enzymes ample in 1.0 ml substrate (65 mmol/ml hydrogen peroxide in 60 mmol/l sodium–potassium phosphatebuffer, pH 7.4) at 37 °C for three minutes. There action was stopped with ammonium molybdate. Absorbance of the yellow complex of molybdate and hydrogen peroxide is measured at374nm against the blank.

## Reagents:

1. Sodium, potassium phosphate buffer (50 mM, pH 7.4): this buffer is prepared by dissolving 1.1g of Na2HPO4 and 0.27g of KH2PO4 in 100 ml distilled water.

2. H2O2 (20 mM) in 50 mmol/l sodium, potassium phosphate buffer: this solution is freshly diluted and standardized daily using a molar extinction coefficient of 43.6 M_1 cm_1 at 240 nm.

3. Ammonium molybdate (32.4mmol/l).

## Calculation

The rate constant of a first-order reaction (k) equation is used to determine catalase activity:

t: time.

S°: absorbance of standard tube.

S: absorbance of test tube.

M: absorbance of control test (correction factor).

Vt: total volume of reagents in test tube. Vs: volume of serum.

## الخلاصة

ثنائي كرومات البوتاسيوم هو مركب كيميائي يحتوي على الكرومات والبوتاسيوم، وهو مادة سامة تستخدم في الصناعات المختلفة كمركب كيميائي ضار. يمكن أن يكون التعرض لثنائي كرومات البوتاسيوم خطراً على البيئة وصحة الإنسان، وقد ثبت أن ثنائي كرومات البوتاسيوم له آثار ضارة على الجهاز التناسلي، ويمكن أن يؤدي التعرض لهذا المركب إلى تلف الخصية وانخفاض إنتاج الحيوانات المنوية لدى الذكور. تشير تقنية النانو إلى استخدام المواد والهياكل بمقياس النانومتر (جزء من مليار من المتر). تتيح هذه التكنولوجيا دراسة المادة والتحكم فيها على المستوى الذري والجزيئي، مما يفتح إمكانيات هائلة في مجموعة واسعة من المجالات. في المجال الطبي، يمكن استخدام تقنية النانو لتطوير الأدوية وإيصالها بدقة إلى المناطق المستهدفة في الجسم، مما يزيد من فعالية العلاج ويقلل من الآثار الجانبية. ويمكن استخدامه أيضًا لتطوير أجهزة طبية دقيقة وفعالة. استكشفت هذه الدراسة الآثار الضارة لثنائي كرومات البوتاسيوم على الجهاز التناسلي الذكري للفئران والدور الوقائي المحتمل للجينسنغ في التخفيف من هذه الآثار. تم تقسيم اثنين وأربعين من ذكور الجرذان البيضاء البالغة إلى سبع مجموعات: مجموعة المراقبة السلبية: تم تلقي محلول ملحي طبيعي يوميًا لمدة 4 أسابيع. مجموعة ثنائي كرومات البوتاسيوم: يُعطى 2 ملغم/كغم من وزن الجسم من ثاني كرومات البوتاسيوم يومياً عن طريق الحقن داخل الصفاق لمدة أسبوعين. مجموعة الجنسنج الإيجابية: تناول الجنسنج عن طريق الفم بجرعة 200 ملجم/كجم من وزن الجسم يومياً لمدة 4 أسابيع. مجموعة نانو الجينسنغ: تناولت نانو الجينسنغ عن طريق الفم بجرعة 200 ملغم/كغم من وزن الجسم يومياً لمدة 4 أسابيع. ثنائي كرومات البوتاسيوم + مجموعة الجينسنغ: يُعطى ثنائي كرومات البوتاسيوم 2 ملغم/كغم + الجنسنغ عن طريق الفم بجرعة 200 ملغم/كغم من وزن الجسم يومياً لمدة 4 أسابيع. مجموعة ثنائي كرومات البوتاسيوم + نانو جينسينج (200 ملجم/كجم): تلقى ثنائي كرومات البوتاسيوم + نانو جينسينج بجرعة 200 ملجم/كجم من وزن الجسم يومياً لمدة 4 أسابيع. مجموعة ثنائي كرومات البوتاسيوم + نانو جينسينج (100 ملجم/كجم): تلقى ثنائي كرومات البوتاسيوم + نانو جينسينج بجرعة 100 ملجم/كجم من وزن الجسم يومياً لمدة 4 أسابيع. تم تحليل عينات الدم لقياس مستويات الهرمون اللوتيني (LH)، والهرمون المنبه للجريب (FSH)، والتستوستيرون، والمالونديالدهيد (MDA)، والكاتلاز (CAT)، وديسموتاز الفائق أكسيد (SOD). تم فحص أنسجة الخصية والبربخ تشريحيا. وكانت النتيجة أن التعرض لثنائي كرومات البوتاسيوم أدى إلى انخفاض كبير في مستويات هرمون التستوستيرون، LH وFSH، مما يشير إلى ضعف وظيفة الخصية. تم أيضًا إحداث الإجهاد التأكسدي، كما يتضح من زيادة مستويات MDA وانخفاض أنشطة CAT وSOD. وكانت هذه التغيرات مصحوبة بتغيرات نسيجية في الخصيتين والبربخ. أدى العلاج بالجينسنغ

أو نانو الجينسنغ إلى تحسين التأثيرات الضارة لثنائي كرومات البوتاسيوم على الجهاز التناسلي الذكري. أعاد كلا شكلي الجينسنغ مستويات الهرمونات، وقللا من علامات الإجهاد التأكسدي، وحسّنا أنسجة الخصية والبربخ. وتشير النتائج إلى احتمال استخدام الجينسنغ كعامل وقائي ضد السمية التناسلية الناجمة عن ثنائي كرومات البوتاسيوم في الفئران.

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**جمهورية العراق**

**وزارة التعليم العالي والبحث العلمي**

**جامعة كربلاء / كلية الطب البيطري**

**فرع الفسلجة والادوية والكيمياء الحياتية**

# تقييم تأثيرات المستخلص الجينسنغ النانوي كمضاد للأكسده في ذكور الجرذان المعرضة لثاني كرومات البوتاسيوم

رسالة مقدمة إلى

مجلس كلية الطب البيطري جامعة كربلاء لاستيفاء جزء من متطلبات

درجة ماجستير في الطب البيطري / الفسلجة

الطالب

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