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Novel biosynthesis of Zinc Nanoparticles Using Dromedary fat and Evaluation of their protective effects against cisplatine induced toxicity and oxidative stress in Wistar rats

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Abstract

Our study aimed to evaluate the therapeutic effect of dromedary fat-capped zinc nanoparticles (DF-ZnNPs) on oxidative stress, immunosuppression, and biochemical disturbances induced by cisplatin (an anticancer chemotherapeutic drug) in rats.

To investigate the biosynthesis of dromedary camel fat-coated zinc nanoparticles, ultraviolet-visible (UV-VIS), Fourier Transform Infrared spectroscopy (FTIR), scanning electron microscopy (SEM), EDX microscopy, transmission electron microscopy (TEM), and gas chromatography-mass spectrometry (GC-MS) were used and an antibacterial activity of these elements was tested.

In an *in-vivo* study 26 male albino wistar rats,6 rats for toxicity testing and 20 rats were randomly divided into four groups (five in each): Control group, Cisplatin group (CP), rats treated with CP and DF-ZnNPs group (CP+ DF-ZnNPs) and rats treated with CP and dromedary fat group (CP+DF). CP induced toxicity using intraperitoneally single dose 5mg/kg. DF-ZnNPs and DF treated intraperitoneally at a dose 5 mg/kg/week in each. Various hematological, biochemical, and oxidative stress markers were estimated. Histopathology of liver, lungs and kidneys tissues was observed.

The results were as expected for the cisplatin group, with mice showing different results compared to the control group. Fluctuations occurred in biochemical parameters (blood sugar $p^{**}<0.01$, cholesterol. Triglycerides ($p^{**}<0.01$, cretin $p^{*}<0.05$, TGO $p^{*}<0.05$, TGP $p^{**}<0.01$) and hematological parameters (RBC, HGB, HCT, MCV $p^{***}<0.001$, MCH. PLT $p^{***}<0.01$, WBC, lymphocytes, granulocytes ($p^{***}<0.001$), as well as oxidative stress in liver, kidney, lung, and heart tissues. As for the treatment regimens, they showed a positive effect in improving biomarkers, reducing oxidative stress, and histological analyses, demonstrating the effectiveness of the nanoparticles.

In conclusion, the observed improvement in the studied parameters encourages the use of the DF ZnNPs as a new treatment accompanying chemotherapy to reduce the symptoms resulting from its secondary effects. Therefore, we need further in-depth studies at the cellular and molecular level to confirm the efficacy of zinc and to ensure the safety of its users from any harm that may occur.

Keywords: Cisplatin, DF-ZnNPs, dromedary fat, Oxidative stress, Liver, kidney, lung

الملخص

هدفت دراستنا إلى تقييم التأثير العلاجي لجسيمات الزنك النانوية المغلفة بدهن الجمل العربي (DF-ZnNPs) على الإجهاد التأكسدي، وكبت المناعة، والاضطرابات الكيميائية الحيوية التي يسببها السيسبلاتين (دواء علاج كيميائي مضاد للسرطان) في الفئران.

لدراسة التخليق الحيوي لجسيمات الزنك النانوية المغلفة بدهن الجمل العربي، تم استخدام الأشعة فوق البنفسجية المرئية (UV-VIS)، ومطيافية تحويل فورييه بالأشعة تحت الحمراء(FTIR) ، والمجهر الإلكتروني الماسح(SEM) ، ومجهر EDX، والمجهر الإلكتروني النافذ(TEM) ، وكروماتوغرافيا الغاز-مطياف الكتلة(GC-MS) ، وتم اختبار النشاط المضاد للبكتيريا لهذه العناصر.

في دراسة أجريت داخل الجسم الحي، تم تقسيم 26 فأر من من ذكور الوستار البيضاء ,6 فئران لاختبار السمية و 20 فأر قسمت عشوائيًا إلى اربع مجموعات(خمسة في كل مجموعة) :(مجموعة الشاهدة، مجموعة سيسبلاتين(CP) ، مجموعة الجرذان المعالجة بـ CP و(CP+ DF-ZnNPs) DF-ZnNPs ، ومجموعة الجرذان المعالجة بـ CP ومجموعة معالجة بدهن الجمل العربي .(CP+DF) تم إحداث تسمم بواسطة CP باستخدام جرعة واحدة 5 ملغ/كغ عن طريق الحقن داخل الصفاق . تم علاج DF-ZnNP و DFعن طريق الحقن داخل الصفاق بجرعة 5 ملغ/كغ/أسبوع لكل منهما .تم تقدير العديد من علامات الإجهاد الدموي والكيميائي الحيوي والتأكسدي .لوحظت أمراض نسيجية في أنسجة الكبد والرئتين والكلى .

كانت النتائج كما هو متوقع لمجموعة السيبلاتين، حيث أظهرت الفئران نتائج مختلفة مقارنةً بالمجموعة الضابطة .حدثت تقلبات في المعايير الكيميائية الحيوية) نسبة السكر في الدم($p^{**}<0.01$) ، والكوليسترول، والدهون الثلاثية($p^{**}<0.01$) ، والكريتين ($p^{*}<0.05$)، و($p^{*}<0.05$) TGO، و ($p^{**}<0.01$) TGPوالمعايير الدموية) نسبة خلايا الدم الحمراء، وHGB، وHCT، وحجم الخلايا المتوسطة($p^{***}<0.001$) (MCV) ، وMCH، و($p^{***}<0.01$) PLT، وخلايا الدم البيضاء، والخلايا الليمفاوية، والخلايا المحببة($p^{***}<0.001$) ، بالإضافة إلى الإجهاد التأكسدي في أنسجة الكبد والكلى والرئة والقلب .أما بالنسبة لأنظمة العلاج، فقد أظهرت تأثيرًا إيجابيًا في تحسين المؤشرات الحيوية، وتقليل الإجهاد التأكسدي، والتحاليل النسيجية، مما يدل على فعالية الجسيمات النانوية.

في الختام، يشجع التحسن الملحوظ في المعايير المدروسة على استخدام جسيمات الزنك النانوية من نوع DF كعلاج جديد مصاحب للعلاج الكيميائي لتقليل الأعراض الناتجة عن آثاره الثانوية .لذلك، نحتاج إلى مزيد من الدراسات المتعمقة على المستوى الخلوي والجزيئي لتأكيد فعالية الزنك وضمان سلامة مستخدميه من أي ضرر قد يحدث

الكلمات المفتاحية: سيسبلاتين،دهن الجمل، DF-ZnNP ، الكبد، الكلى، الرئة، الإجهاد التأكسدي.

ABBREVIATIONS LIST

ALAT: alanine aminotransferase

ASAT: aspartate aminotransferase

CP: Cisplatin

DF-ZnNPs: Zinc oxide synthesised by dromedary Fat

DMSO: Dimethyl Sulfoxide

EDTA: Ethylenediaminetetraacetic acid

EDX: Energy dispersive X-ray

FTIR: Fourier Transform Infrared spectroscopy

GC-MS: Gas chromatography–mass spectrometry

GSH: glutathione

GSH-Px: glutathione peroxidase

GSSG: glutathione disulfide

H2O2: Hydrogen hydrogen

Hb: hemoglobin

Hct: hematocrit test

HGB:hemoglobin level

iNPs: inorganic nanoparticles

MCH:mean corpuscular volume

MCHC:mean corpuscular hemoglobin concentration

MCV:mean Corpuscular Hemoglobin

MDA: malondialdehyde.

NADPH: nicotinamide adenine dinucleotide phosphate

NPs: Nanoparticles.

PBS: Phosphate-Buffered Saline

PLT: Platelets

RBC: Red blood cells

ROS: Reactive oxygene species

SEM: Scanning electron microscope

SOD: Superoxide dismutase

SOD: superoxide dismutase

TC: cholesterol

TEM: Transmission electron microscopy

TG: triglycerides

UV : Ultraviolet Radiation

UV-VIS: Ultraviolet-visible spectroscopy

UV-Vis : Ultraviolet–visible

VLDL: very low-density lipoprotein

WBC: White blood cells

ZnONPs : Zinc oxide nanoparticles

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Introduction

Introduction

One of the leading causes of mortality worldwide, cancer accounts for millions of deaths annually **(Zhu et al., 2025)**. It's has yet been represented as the second cause of death worldwide after cardiovascular disease **(Afrouz et al.,2023)**. With a staggering 28 million new cases per annum estimated by 2040 **(Tillman et al.,2025)**. The rest of the patients do not recover from this disease. Among all kind of cancer treatments, chemotherapy has emerged as a pivotal treatment strategy **(Gu et al.,2025**). The use of chemotherapy has proven effective in treating not only solid tumors but also hematologic malignancies, enhancing preoperative conditions and lowering postoperative recurrence rates, thus improving overall survival **(Yuan et al.,2024).** Alkylatingdrugs are chemotherapeutic agents given against most of the cancer types Mainly includes platinum drugs" cisplatin "(CP) , which interfere with the formation/linkage of DNA double strands. These drugs can cause it by transferring one alkyl group to the guanidine base in DNA **(Anand et al., 2023).** On the other hand, the permanent use of cisplatin has many side effects, such as kidney disorders, allergic reactions, reduced immunity to infections, gastrointestinal diseases, bleeding, and hearing loss **(Salcan et al., 2025)**, toxicity against liver, heart (**Ghosh ,2019),** nephrotoxicity (kidney damage) due to the excretion of the drugs through the kidneys.

These challenges underscore the urgent need for more precise, effective and less toxic therapeutic approaches. To overcome these drawbacks, Numerous of nanotechnology techniques in biomedical research are designed **(Ghasemian et al., 2023**). Nanotechnology represents a revolutionary path for technological development that concerns the management of material at the nanometer scale (one billion times smaller than a meter).

Zinc nanoparticles are gaining increasing attention for their applications in various fields, such as medicine, electronics, and environmental remediation. By using natural extracts in their production, researchers can follow a more environmentally friendly approach that avoids the toxic chemicals common in traditional synthesis methods (**Derouiche et al., 2022; Kumar &Yadav,2014)**. The green synthesis approach to creating NPs has gained tremendous strides as an alternative to physical and chemical syntheses. Where eco-friendly bioactive agents are employed in NP synthesis.as the byproducts and capping agents are natural to the

environment, which is highly beneficial in the medical sector. In an attempt to reduce chemicals in treatments and mitigate their side effects and associated toxicity **(Venkatas et al.,2022)**. The use of natural recourses eliminated the necessity of toxic chemicals for the large-scale preparation of advanced metal nanoparticles **(Nejad et al., 2024**).

Camel fat, particularly from the camel hump, has received attention for its unique composition and potential health benefits. Research suggests that camel fat has a favorable lipid profile **(Bakry et al., 2021),** a complex mixture of natural lipids (triglycerides, phospholipids, cholesterol, and other elements) **(Haddad et al., 2010**), and the essential fatty acids valerian and linoleic (Nuyar et al., 2010), as well as vitamins A and E **(Bakry et al., 2021)**.Also, the thermal stability of camel fat allows undergo biosynthetic reactions at relatively high temperatures (40–60°C) without degradation of the lipid matrix, enhancing the reaction kinetics (**Rahman et al., 2019**).

This work aims to evaluate the therapeutic effect of dromedary fat, a well-known component in traditional medicine. To enhance its therapeutic efficacy, dromedary fat, a natural product, was combined with zinc oxide nanoparticles using nanotechnology techniques, resulting in the formation of dromedary fat-zinc nanoparticles (DF-ZnNPs).

Based on the previous outcomes, a dual approach was adopted to conduct a comprehensive study combining:

In-vitro part: it consists of a biosynthesis of zinc nanoparticles by using dromedary fat along with quantitative and qualitative characterization of these compounds and evaluation of their biological property. *In-vivo* part: it was about evaluation of the preventing efficiency of DF-ZnNPs and dromedary fat against metabolic, physiological and histological changes induced by Cisplatin in rats.

First part

Bibliographic synthesis

Chapter I

Cisplatin

1.Chemotherapy

1.1. Definition

Chemotherapy treatments are used to inhibit vigorously growing malignant cells with anticancer agents **(Alam, 2018**). It is classified based on therapeutic goals into neoadjuvant, adjuvant, curative, and palliative chemotherapy **(Noronha et al.,2024**). It's often used in combination with other therapies, such as surgery, radiation, or hormone therapy. Usually, cancer drugs work by damaging the RNA or DNA that tells the cell how to copy itself in division (**Kaur et al., 2022**). Chemotherapy drugs can activate multiple signaling pathways and augment the secretion of inflammatory mediators **(Behranvand et al.,2022**). Cancer cells usually divide and grow at a much-accelerated rate than normal cells and are physiologically possess very high endogenous stress. Therefore, the drugs can destroy them rapidly and more effectively in comparison to other surrounding cells (**Dewanjee et al., 2023**). there are several different classes of anticancer drugs based on their mechanisms of action, and they include the following:

a) alkylating agents which damage DNAb) anti-metabolites, antibiotics d) topoisomerase inhibitors that inhibit either topoisomerase I or II, e) mitotic inhibitors that inhibit mitosis and cell division.f) corticosteroids **(Huang et al., 2017**).Examples include drugs used in chemotherapy, such as:Chlorambucil , Cyclophosphamide, Busulfan ,5-fluorouracil (5-FU) ,6mercaptopurine (6-MP), Doxorubicin،Dactinomycin ،Eribulin ،Paclitaxel ،vinblastine and and cisplatin (**Anand et al.,2023**).In this chapter we focused on the study of cisplatingreatly advanced tumor chemotherapy. Furthermore, almost 50% of cancer patients choose cisplatin for commencing chemotherapy (**Galanski et al.,2023**).

2. Cisplatin "Chemotherapy"

2.1. Definition and indication of Cisplatin

cisplatin, known alternatively as cis-diamminedichloroplatinum (II) or cis-diammineplatinum (II)(**Li et al., 2024**) is a chemotherapeutic agent (**Szefler and Czeleń, 2023),**antineoplastic in the class of alkylating agents and is used to treat various forms of cancer **(National Center for Biotechnology Information [NCBI], 2025)**. CP is a first-generation platinum drug containing two chloride ligands in the cis configuration **(Kopacz-Bednarska & Król, 2022)**. It has also been modified to create other platinum-based drugs, such as carboplatin and oxaliplatin, which have different properties and side effects **(Elmorsy et al., 2024**). Cisplatin exerts anticancer activity via multiple mechanisms but its most acceptable mechanism involves generation of DNA lesions by interacting with purine bases on DNA followed by activation of several signal transduction pathways which finally lead to apoptosis **(Ghosh, 2019)**. Clinically, it has been proven to combat different types of cancers including sarcomas, cancers of soft tissue, bones, muscles, and blood vessels **(Esmail et al., 2019)**, testicular, bladder, breast and lung **(Perše, 2021)** lymphomas, and germ cell tumor **(Srinivasan et al., 2016)**. gastrointestinal tract, and brain **(El-Sheikh & Khired, 2023)**. Moreover, that is used for the treatment of various solid tumors, such as lung cancer, stomach cancer, and ovarian cancer **(Fang et al., 2021)**,and for the treatment of tumors in children, such as neuroblastoma, osteosarcoma, and hepatoblastoma **(Tan &Vlajkovic ,2023)** First-line chemotherapy for head and neck, esophagus, gastric, colon, , and cervix cancer ,the second cytostatic towards advanced small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC), breast, pancreatic, liver, kidney, and prostate cancer **(Tsvetkova & Ivanova ,2023)**. In hyperthermic intraperitoneal chemotherapy (HIPEC)Cisplatin is employed after cytoreductive surgery (CRS) for peritoneal surface malignancies (PSMs) **(Grillo-Marín et al., 2024**).

2.2. Chemical structure

Cisplatin (CAS no. 15663-27-1, MF-Cl2H6N2Pt; NCF-119875)**(Dasari & Bernard Tchounwou, 2014)** is a square–planar complex with two labile chloride (Cl) ion ligands and two relative inert ammonia (NH3) ligands coordinated to the central platinum (Pt) atom in a cis configuration **(Zhang et al., 2021)**.CP is the cis-isomer of [PtCl4(NH3)2].It is an orange-yellow or bright yellow crystalline powder stable at room temperature, slightly water-soluble, and

soluble in dimethyl primanide and N, N-dimethylformamide. The specific square-planar geometry of cisplatin renders it sufficient to inhibit cell division in bacterial and biologically active to kill tumor cells, unlike its anti-tumor ineffective trans isomer **(Wang et al., 2023).**The molecular formula of cisplatin is Cl2H6N2Pt, molecular weight of 301.1 gm/mol, a density of 3.74 g/cm3, a melting point of 270 °C, a log Kow of −2.19 and a water solubility of 2.53 g/L at 25 °C **(Ali et al.,2022)**.The chemical stability of cisplatin solution also depends on its pH and the influence of sunlight. The preferable pH of the solution of proved stability ranges between 3.5 and 5.5. Cisplatin is also relatively sensitive to light **(Karbownik et al., 2012)**.

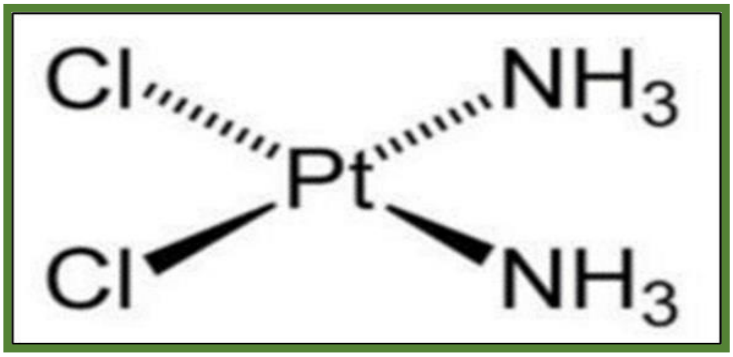

Figure 01: Chemical structure of cisplatin drug **(Dasari et et al 2022)**

2.3. Pharmacokinetics

Pharmacokinetics relates to processes from drug absorption to its elimination from the body. This is commonly referred to as the so-called ADME scheme **(Ott, 2013)**. It describes how the body's systems biologically affect medicines. To prevent, control, and treat diseases **(Moini et al., 2023)** in case of treatment with cisplatin, reduced uptake of the drug and increased efflux has been observed, leading to drug resistance. As mentioned earlier, CTRs (copper transporter proteins) play a vital role in cancer resistance against cisplatin **(Dasari et et al 2022)**.

2.3.1Administration

Cisplatin is administered to cancer patients by intravenous (i.v.) injection. Based on the insufficient stability of the drug in aqueous media, the injection solutions are freshly prepared shortly before use **(Ott, 2013)**. The volumes and durations are minimum administration standards to accommodate the wide variation in clinical practice in delivery of cisplatin. They should be individualized, based on the clinical situation which may affect the hydration regimen and addition of electrolytes. In children, for moderate to high-dose cisplatin **(Matysiak & Gustaw**

,2009). Administer with caution to individuals with pre-existing renal impairment, myelosuppression or hearing impairment. Lower doses of cisplatin are given with less intensive hydration,hydration is required to minimize nephrotoxicity **(Murry, 1997)**.Also, cisplatin is available in the form of sterile, unpreserved, single-dose vials [10 mg/10 mL, 50 mg/50 mL and 100 mg/100mL] at a concentration of 1 mg/mBalis L **(Woollins et al., 1983, Balis et al., 1983)**.

2.3.2. Absorption

Cisplatin itself is a rather polar molecule and consequently its uptake is relatively slow and takes place over extended exposure periods **(Ott, 2013).**

2.3.3. Distribution

Cisplatin reaches systemic circulation within 10 min after systemic administration (ip, iv) **(Perše, 2021)**. intravenous drug is rapidly distributed in tissue, with tissue half-life of 2-4 days **(Edelman & Rupard, 2006)** distributes to the kidneys, liver, and intestines, but does not penetrate the blood brain barrier and the volume of Distribution 11.5l/m2 **(Reece et al.,1987)**.Cisplatin does not bind irreversibly to plasma proteins, but platinum does form a tight complex **(DeConti et al.,1973)** .The extensive protein binding of platinum species in plasma is a time-dependent interaction, with the bound fraction increasing to more than 90% over 2 to 4 hours **(Balis, 1986).** once entered into the cell, cisplatin undergoes hydrolysis of the two chloride ions, producing a cis-diaminodiaquo complex that is involved in DNA adduct formation and cytotoxicity **(Di Francesco et al., 2002)**, and it reacts with intracellular molecules, such as DNA, proteins, and GSH, forming covalent adducts **(Elmorsy et al., 2024)**.

2.3.4. Elimination

Cisplatin is eliminated quickly following a biphasic process. The major route of elimination is renal (25–50%) **(Ott, 2013)** through glomerular filtration and tubular secretion **(Miller et al., 2010)**, much less by biliary **(Siddik et al.,1987),** or intestinal excretion. It appears that the rate of cisplatin clearance in repeated treatment depends on the dose (cumulative) and the frequency interval (daily vs weekly) **(Esteban-Fernández et al.,2008).**

2.4. Mecanisme of action Cisplatin

Cisplatin acts via cell cytotoxicity **(Riddell,2018)**, As a platinum-based compound, cisplatin is inert but is activated through a Series of aquation reactions **(el-Khateeb et al.,1999)**. The aquation process involves the spontaneous Substitution of one or both cis-chloro groups with water molecules in the Cytoplasm **(Kelland,2000) (figure).**

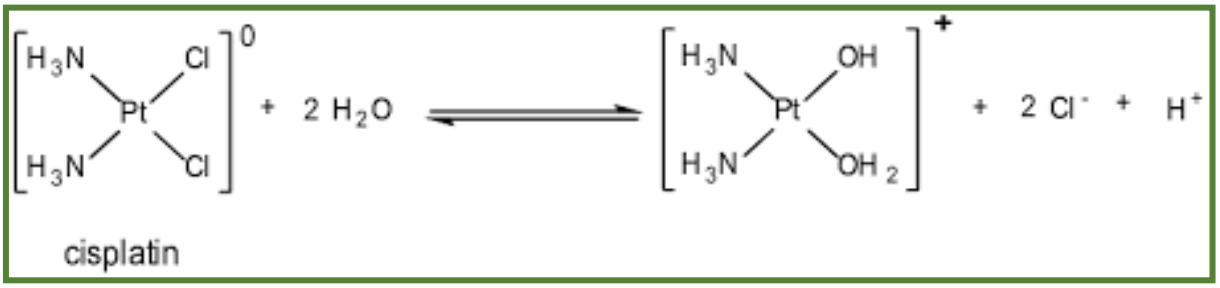

Figure 02: Hydrolyse of cisplatin to generate the active form **(Bradford & Cowan,2014)** .

This process makes aquated cisplatin highly reactive Toward intracellular nucleophiles **(Michalke,2010)**. It is this process that yields the Anticancer effects of cisplatin through reactions within the cytoplasm and nucleus. Within the cytoplasm, cisplatin reacts with nucleophiles such as Methionine, metallothioneins, reduced glutathione (GSH) and proteins via Cysteine residues **(Berndtsson et al.,2007)** .

Hydrolyzed cisplatin interacts with high affinity with the nucleophilic N7 sites of purine bases to form inter- and intrastrand crosslinks of DNA **(Eastma,1987)**. These lesions distort DNA structure, triggering multiple DNA damage signals **(Bellon & Lippard,1990**). One of the triggered signals involves the nucleotide excision repair (NER) complex. This system recognizes denatured DNA and attempts to remove the addition products to enable cell survival **(Furuta et al.,2002)**. Other DNA damage signals include the mismatch repair (MMR) and base excision repair (BER) systems. In this case, components of these complexes sense DNA lesions and initiate signaling that determines cell fate (**Dianov & Hubscher, 2013)**. Thus, the cell will initially attempt to repair the cisplatin-induced DNA lesion through one of the DNA repair mechanisms. However, the toxicity of cisplatin depends on the widespread availability of the added compounds, as well as the high tumor proliferation rate **(Appella & Anderson,2001).** This makes DNA repair largely impossible. As a result, cell death occurs. The key link between DNA damage and apoptosis involves the Rad3-related telangiectasia transforming (ATM) kinase (ATR) and checkpoint kinase 1 (CHK1). Cisplatin-dependent sequential activation of ATR and

CHK1 leads to the activation and stabilization of the tumor suppressor protein p53 through phosphorylation at serine 20 **(Zhao & Worms, 2001**).

p53 is a central mediator of cisplatin-induced apoptosis. In cisplatin-sensitive cells, **(Delmastro et al .,1996).**it also upregulates several apoptosis-inducing genes, including NOXA**(Oda et al.,2000)**, and Bax **(Hershberger et al.,2002)**.These apoptosis-inducing factors are involved in the initiation of the mitochondrial intrinsic complex apoptosis pathway **(Kroemer et al.,2007)**.Cisplatin induces p53-mediated localization of NOXA and Bax to mitochondria leading to the release of cytochrome c that activates caspase-dependent apoptosis **(Chai et al.,2000)**. **(Figure 06)**.

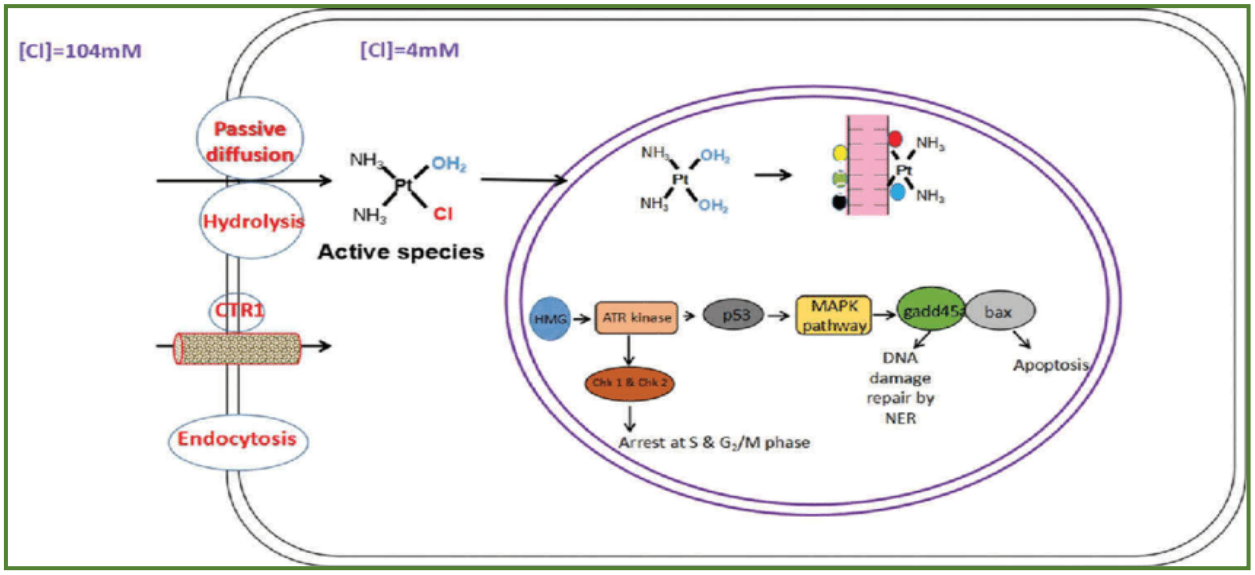

Figure 03: Schematic representation of mechanism of action of cisplatin **(Jain et al.,2017).**

Chapter II

Camel and fat

1. Definition

Camel is one of the oldest animals domesticates as documented in ancient history and the name is derived from the Latin (Camelus) and Greek (Kamélos) languages **(Gaughan,2011).** Camels are a cultural, economic, and health icon, with a global population estimated at more than 35 million **(Bakry et al., 2021**). They provide meat, milk, fat, transportation, and other essential services **(Faye et al., 2014)** Camels possess unique physical Characteristics that enable them to thrive in Challenging environments characterized by High temperatures, intense solar radiation, And limited food and water resources **(Kurtu, 2004)**. From its astounding adaptations that Enable survival in harsh environments to its Pivotal role in trade and transportation, **(Hussain et al., 2016)**. The Camel exemplifies a true miracle. Camels Fulfill a crucial economic function in arid and semi-arid regions worldwide **(Faye, 2020)**. The camel, often hailed as the "ship of the desert," holds a profound place in the hearts and lives of people residing in arid regions **(Burger et al.,2019**). Camels contribute hugely to human survival in less agroecological parts of African, Asian and Arabian deserts. They have been used for transportation, as a source of food and for protection for a very long time. Nowadays, they are hugely important in many parts of the arid world as sustainable livestock species **(Burger,2016**).

2. Historically

camels were widely used as a principal mean of transport of humans and goods between countries, **(Bornstein, 1990)**. Recently, additional uses of camel have emerged including tourism, racing events and beauty contests, all emphasizing the fact that camel is a precious multipurpose animal **(Faye, 2015)**. Several attempts have been carried out to understand the mystery of camel adaptation and the incredible capability of camel to withstand dehydration, thermal stress and other harsh environmental conditions **(Ouajd & Kamel,2009; Gebreyohanes & Assen, 2017)**. A distinctive coordination of anatomical, physiological and behavioral criteria is found to play a role in such efficient adaptation.

3. Anatomically

several adaptations have been identified: the one humped camel is provided with a single hump filled with fat rather than the common belief of being filled with water **(Mohammed et al., 2005**). The high fat content in camel humps serves as an energy store which is used in

periods of food limitation **(Chilliard, 1989**). Camel nostrils have a muscular nature which allows camel to fully control its opening and closure, thus avoiding sand inhalation in case of sandstorm events **(Gebreyohanes & Assen, 2017**). The feet of camel are thick and characterized by leathery pads which spread widely on hitting the ground, consequently preventing the animal from sinking into the warm sand. Camel legs are long compared to other desert animals and during walking each two legs move on one side, rocking side-to-side, therefore giving another reason for being nicknamed the ship of desert. Among the interesting internal anatomical features observed in camels is the unique water sac structure in the stomach serving to store water **(Allouch, 2016)**. Interestingly, the anatomical arrangement or distribution of camel arteries and veins help mitigate the high blood temperature of the body reaching the brain, thus protecting the animal from potential brain damage. This mechanism is referred as "selective brain cooling" **(Ouajd & Kamel, 2009)**. Suprisingly, camel RBCs possess distinctive membrane phospholipid composition, resulting in a more fluid membrane, and enabling them to bear high osmotic variations without rupturing even in cases of rapid rehydration **(Warda & Zeising 2000; Warda et al.,2014)**.

Moreover, Genetic studies of the camel have elucidated the role of several genes that enable them to adapt to desert conditions **(Agrawal,2011)**, Importantly, several studies have uncovered the beneficial property of camel products in the treatment of various diseases (**Jirimutu et al.,2012)**.

4.Classifiction

they first evolved in North America **(Rybczynski et al., 2013)**. In time, the camels evolved into a number of species of the camel family Camelidae (camelids). The Camelidae family consists of two genera: Camelinae and Laminae. The genus Camelinae comprises two domestic species: Camelus dromedarius (also known as the one-hump camel or Arabian camel, and Camelus bactrianus (also known as the two-hump camel or Bactrian camel) **(Burger, 2016) (figure1).**

4.1. Camelinae

4.1.1. Camelus dromedarius

The Arabian camel first appeared in southern Arabia around 4000–3000 BC, mainly **(Monchot, 2015**). Then migrated from the Arabian Peninsula to South Asia and the African continent **(Almathen et al., 2016)**. Today, Arabian camels form an important part of the domestic livestock in most arid regions of Africa, the Middle East and South Asia. Bactrian camels are distributed mainly across deserts and semi-deserts in northern and northwestern China, throughout Mongolia and parts of Central Asia **(Kazakhstan and Russia**). Some Bactrian camels also live in India, Pakistan, Afghanistan and Iran. A remnant population is found in Turkey and Crimea **(Zarrin et al., 2020).** Known types in this group are as follows.

4.1.1.1. Marecha: This type originated in Pakistan and is named after Marecha tribe from the desert of Pakistan. This type has real production potential for milk.

4.1.1.2. Al-Majahim: Al-Arabia: This is also called Al-Njdeiah. It originated in Saudi Arabia especially in Najd and Dawaser Valley in the north and northeast of Saudi Arabia.

4.1.1.3. Sirtawi: This is found mainly in the Sirt area in the middle coastal zone in Libya **(Faraz et al., 2018)**.

4.1.2. Camelus bactrianus

Camelus bactrianus (also known as the two-hump camel or Bactrian camel). The wild Bactrian camel fromTartarian desert (Mongolian-China border). Mongol Several ecotypes are described In China, five ecotypes are recorded while three are described in Mongolia. Among Mongol group, Alxa breed) is the higher Dairy producer (on average 650 L/lactation). Alxa camels can be found in the Alxa county in China, but also in northern Afghanistan, Tajikistan, and parts of Mongolia **(Zhang et al., 2005)** is defined as genetically different as domesticated Bactrian and named Camelus b. Ferus **(Butt & Asim.2023**). The singlehumped camel (Camelus dromedarius), the Double-humped camel (Camelus Bactrianus), and the endangered camel Species (Camelus ferus) have extensive Distributions across various regions, Including Africa, the Middle East, Central Asia, China, as well as remote areas of Mongolia and Northwest China **(Burger et al., 2019**).

4.2. Laminae

The Lama genus comprises four species: Lama glama (llama), Lama pacos (alpaca), Lama guanicoe (guanaco), and Lama vicugna (vicuna) **(Zarei Yam & Khomeiri,2015**).

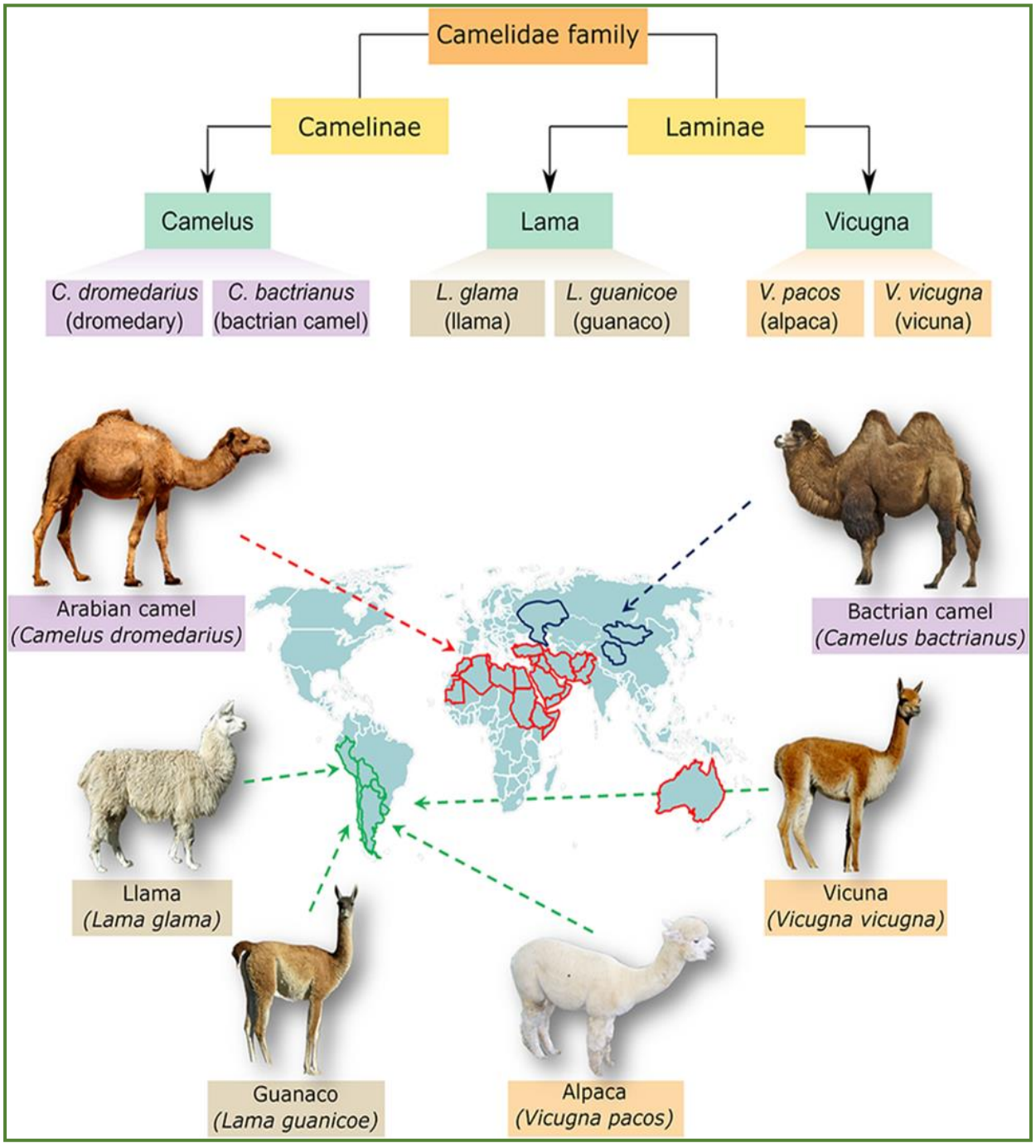

Figure 04. Classification and distribution of camel species **(Hoter & Naim.,2019**).

5.Camel fat

Animal fat plays an important role in human nutrition **(Fleming, 2002).** Camels store energy as fat deposits accumulated in various parts of the body, mainly hump and abdomen **(Kadim et al, 2002**). The hump contains most of the subcutaneous fat, while the internal fat is mainly located around the kidneys (15 % of the fat storage) and inside the mesentery (5%) **(Kamili et al, 2006**). Camel fat, particularly from the camel hump, has received attention for its unique composition and potential health benefits. Research suggests that camel fat has a favorable lipid profile **(Bakry et al., 2021**), the weight of lipids in the hump is estimated between 10 and 20 kg, but with a large variability associated to the physical activity and the nutritional and physiological status, age and sex of the animal **(Wilson, 1984**).

5.1. Composition

Camel hump fat contains multiple and complex fatty components, a complex mixture of natural lipids (triglycerides, phospholipids, cholesterol, and other elements) **(Haddad et al., 2010**), which represent the basic energy that camels rely on to survive in harsh environments **(Emmanuel & Nahapetian, 1980**), which are mostly secreted in the form of triglycerides or phospholipids **(Kadim et al.,2012**), as it consists of saturated fatty acids represented by palmitic acid and citric acid, while unsaturated fatty acids include oleic acid and linoleic acid **(Haussman,1998**). In addition, hump fat contains antioxidants such as tocopherols (vitamin E), vitamins A **(Bakry et al., 2021**). which contribute to reducing oxidative reactions **(Jassim et al.,2018)**, as well as omega6 **(Sahraoui et al.,2015).** Fortunately, the emerging properties of camel fat due to low cholesterol and high-unsaturated fatty acids content **(Mashaly et al.,2020)** provide the foundation for the expansion as a healthy fat in the human diet. represents promising alternative **(Muzzachi et al.,2015).**

5.2. Pharmacological effect

5.2.1. Protection from ultraviolet rays

A study by **(Jassim et al., 2018)** showed that camel hump oil contains saturated fatty acids, omega 3, 6, and 9, and vitamin E, which give it UV-protective properties. It has been shown to be effective in protecting the skin of mice from UV-induced damage.

5.2.2. Reduce muscle spasm

According to a study **(Kalantari et al., 2017**), camel hump oil was found to reduce muscle tension due to its combination of fatty acids, including citric acid, stearic acid, oleic acid, and myristic acid, as well as several triglycerides, giving this oil unique properties. The effect of camel hump oil is due to the triglycerides, which improve the skin barrier, regulate skin temperature, and positively impact growth.

5.2.3. Softening leather

Camel hump fat has been used as a leather softener, improving its elasticity and quality **(Habib et al., 2022)**.

Chapter III

Nanotechnology

1. Nanotechnology

Nanotechnology represents one of the most transformative fields in modern science **(Khan, 2022)**, Nanoscience break throughs in almost every field of science and nanotechnologies make life easier in this era. The National Nanotechnology Initiative (NNI) defines nanotechnology as the manipulation of matter within dimensions ranging from 1 to 100 nanometers, affecting its properties at the atomic, molecular, and macromolecular levels **(Khatoon & Veledandi, 2025)**. It is a process that combines the fundamental properties of biological, physical, and chemical sciences. These processes occur at the precise nanometer scale. Physically, size is reduced, chemically, new bonds and chemical properties are controlled, and biological effects are produced at the nanoscale, such as drug binding and delivery at specific sites **(Malik et al., 2023)**. The notion of nanotechnology was initially articulated by the esteemed Nobel Laureate Richard Feynman at his renowned lecture at the California Institute of Technology on December 29, 1959. Where he presented the top-down way of designing nanomaterials **(Periakaruppan et al., 2023**). Their applications have revolutionized multiple sectors through the manipulation of matter at the nanoscale, leading to the creation of innovative solutions with unprecedented capabilities, including catalysis, energy storage, agriculture, and medicine **(Sim & Wong, 2021; Joudeh & Linke, 2022)**, and environmental applications with nanomaterial-based solutions for water purification, pollutant removal, and pollution monitoring **(Zhang et al., 2023**).

Nanotechnology has opened up new possibilities in medicine for targeted drug delivery that enhances therapeutic efficacy while minimizing side effects, while nanodiagnostics offer exceptional sensitivity for disease detection **(Singh & Mehta, 2024**). They are also being used in surgery, analytics, dermatology, neurology, and other branches of medicine to help transport diagnostic and therapeutic agents across biological barriers, ensure access to specific molecules, mediate specific molecular interactions, or detect changes in molecules of interest **(Karahmet Sher et al., 2024**).

2. Nanoparticles (NPs)

A nanoparticle is usually defined as a particle of matter that is between 1 and 100 nm **(Patil et al., 2021)**.At this scale, materials exhibit unique physical, chemical, and biological properties that differ significantly from their bulk counterparts due to quantum effects and their high surface area-to-volume ratio **(Yameny, 2024)**.A nanoparticle is a solid colloidal particle(Maxwell al., 2021)Based on their dimensionalities, nanomaterials categorize into four different classes 0D,1D,2D,3D **(Joudeh & Linke.,2022**).The properties of the particles and their structures are the significant feature determine the functionality, activity, and utility of the NPs. For example, the size and the shape of nanoparticle can determine the modification possibilities, optical characteristics, and its entry to cells **(Eker et al., 2024**). Nanoparticles have many applications such asindustry,diagnostics,antimicrobials,drug delivery, the agriculture industry, the food industry…etc **(Altammar, 2023).**

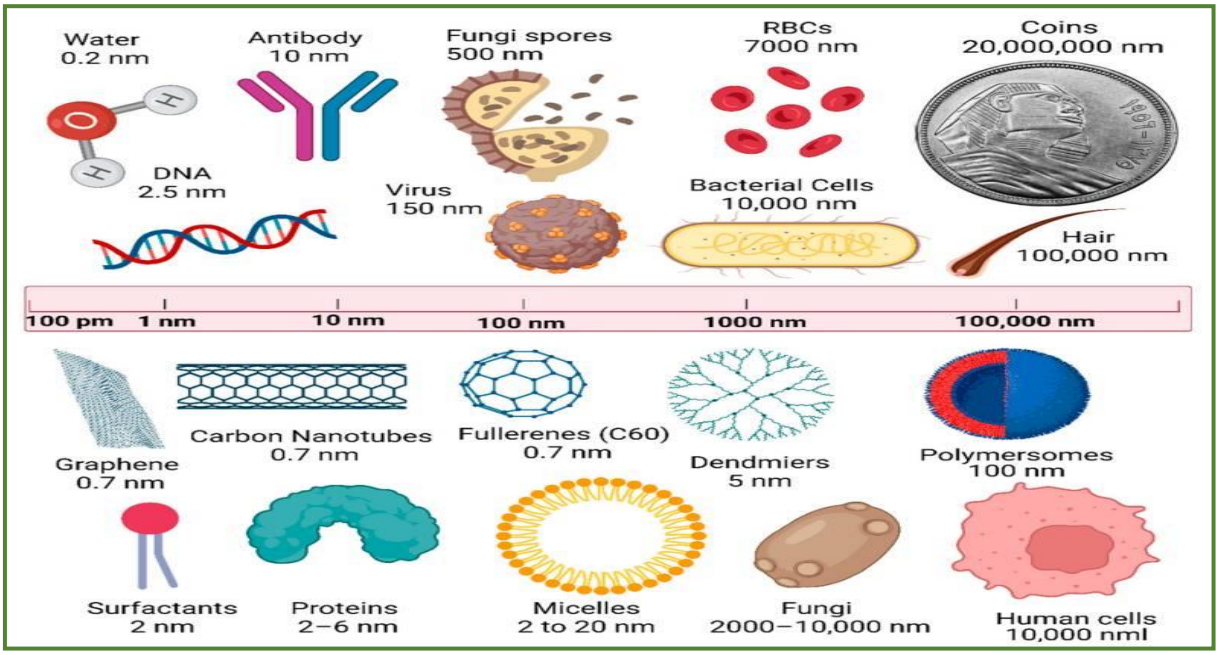

Figure 05: Size comparison of various objects in the nanoscale regime **(Barhoum et al.,2022)**.

3.Classification of nanoparticle

There are three categories into which nanoparticles are normally divided **(Jyoti et al.,2023) (Figure 03**).

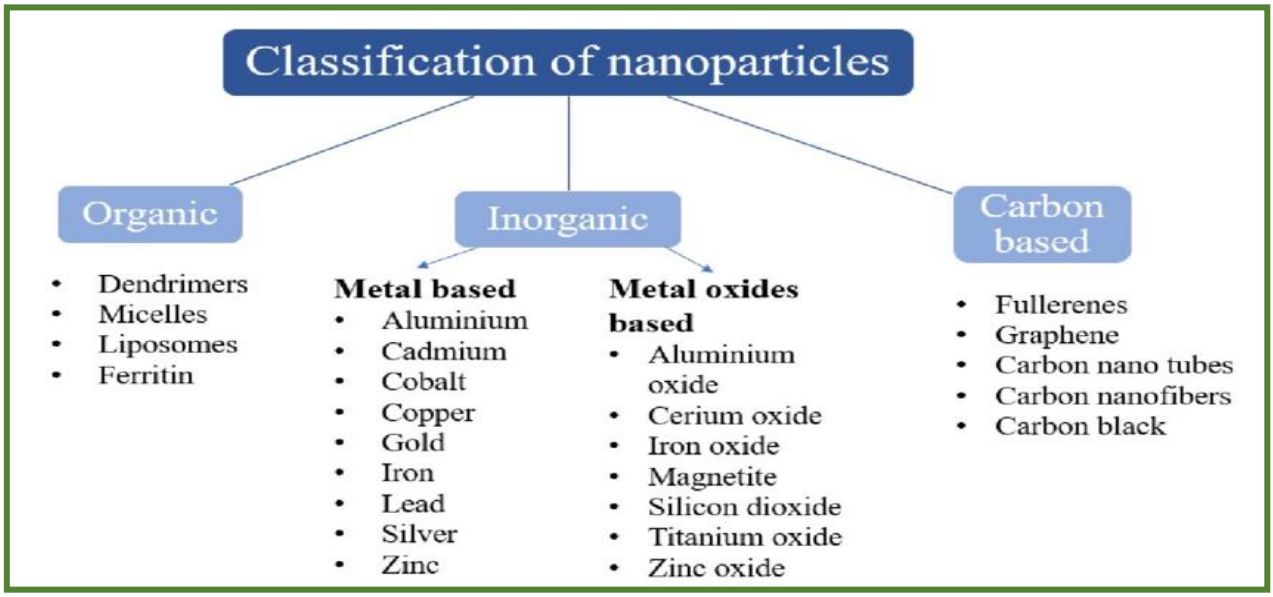

Figure 06 : Classification of nanoparticles **(Jyoti et al., 2023**).

3.1. Organic Nanoparticles

Organic nanoparticles can be commonly described as solid particles made of organic compounds **(Kumari & Sarkar, 2021)**, they are including dendrimers, micelles, liposomes and ferritin **(Jyoti et al., 2023).** Organic NPs demonstrate significant attributes like non-toxicity and biodegradability **(Eker et al.,2024)**, tunable surface chemistry **(Mitchell et al., 2021)**, also are commonly employed in the process of transporting target medications to their intended locations **(Alshammari et al.,2024)**.

3.2. Carbon-based nanoparticles

Nanoparticles whose skeletons are wholly organized from carbon are referred to as carbon-based NPs **(Zahoor et al., 2021)**, which have been categorized into graphene, fullerenes, carbon nanofibers, carbon nanotubes, black carbon **(Jyoti et al., 2023**). In particular, carbon nanomaterials have many potential biomedical applications, including imaging biosensors, anticancer drugs, drug delivery vehicles, and bioengineering **(Holmannova et al.,2022)**. All the nanomaterials based on carbon possess some notarious inherent properties, such as high electrical

conductivity, chemical stability, high surface to volume ratio and biocompatibility **(Fritea et al.,2021)**.

3.3. Inorganic Nanoparticles

Inorganic NPs (iNPs) are composed of inorganic atoms associated with covalent or metallic relations **(Eker et al.,2024)**. Inorganic nanoparticles have the advantages of being hydrophilic, non-toxic, and biocompatible with living systems. The stability of inorganic nanoparticles is superior to that of organic nanoparticlesrelations **(Alshammari et al.,2023).**

3.3.1. Metal Nanoparticles

Metal-based nanoparticles, synthesized from different metals **(Vikram et al., 2023)** like Aluminium, Cadmium, Cobalt, Copper, Gold, Iron, Lead, Silver and Zinc **(Jyoti et al., 2023**). The synthesis of metal nanoparticles is controlled by shape, facet, and size. (Ijaz et al.,2020). They have unique properties based on their size and characteristics, including expanded surface area, pore size, the density of charge on the surface, cylindrical and spherical shape, color, amorphousness, and crystalline structures. Environmental factors, including air, heat, sunlight, and moisture, also affect NPs properties **(Zahoor et al.,2021).**

3.3.2. Metal oxides Nanoparticles

Metal oxide nanoparticles such as Aluminium oxide, Cerium oxide, Iron oxide, Magnetite, Silicon dioxide, Titanium oxidem and Zinc oxide represent notable examples of inorganic NPs **(LewisOscar et al., 2016**). Metal oxide NPs are synthesized by modifying the properties of their corresponding metals **(Burlec et al., 2023)**. Over the past few decades, there has been increasing scientific intrest in metal oxide nanoparticles **(Khan et al., 2022)** due to their excellent properties **(Negrescu et al., 2022)**. These nanoparticles have a very high surface-to-volume ratio, high pore volumes, flexible pore size, effective surface properties, and high thermal stability when compared to other conventional formulations and microparticles **(Yadav et al., 2022)**.Furthermore, due to their reduced size, metal oxide nanoparticles can interact on a more in-depth level with various cellular structures they do not cause systemic toxicity due to their highly improved biocompatibility **(Rostami et al., 2021, Biswas & Bellare, 2022)**.Some typically integrated metal oxide Nanoparticles incorporate zinc oxide (ZnO) **(Ealia & Saravanakumar, 2017)**have shown significant potential across wide range of applications, including

photocatalysis, drug delivery, antimicrobial coatings, environmental remediation, and energy storage **(Khan et al., 2019)**.

4.Zinc oxide nanoparticles (ZnO NPs)

Zinc plays a vital role in the supportive essential cellular procedures due to being one of the critical trace elements in the organism of human and substitute as a co-factor of more than 300 enzymes **(Abass & Abdoon, 2024)**. It contributes to several fundamental biological processes, including immune system regulation, protein synthesis, wound healing, DNA replication, and cell division. Notably, zinc is indispensable for the production of red blood cells,that is why a deficiency in this metal can cause anemia. Given that the human body lacks the capacity to store zinc, it must be obtained consistently through dietary intake to ensure the maintenance of these vital physiological functions **(Islam et al., 2023)**.

Zinc oxide (ZnO) is an inorganic metal oxide with a vast range of nanostructures. their low cost, large surface area **(Khan et al, 2022)**. Zinc oxide nanoparticles (ZnO-NPs) are one of the metal oxide nanomaterials and a valuable and versatile inorganic compound due to its unique physical and chemical characteristics **(Zhou et al., 2023)**. ZnO-NPs display properties that are distinct from those of typical NPs **(Faisal et al., 2021)**. Such as their biocompatibility and non-toxicity **(Islam et al., 2022)**, their low cost, large surface area **(Khan et al, 2022)**. Moreover, ZnO NPs exhibit a strong antibacterial effect, mainly attributed to their distinct characteristics, that is also dependent on dose, time and synthesis method **(Mirzaei & Darroudi, 2017)**. make them an excellent choice for use in many domains **(Ben Chobba et al., 2024)**. In the biomedical field, they have received attention due to their high biocompatibility with human cells **(Jha et al., 2023)**. ZnONPs were found to be biocompatible using human erythrocytes and macrophages **(Iqbal et al., 2021)**. In addition, it has great potential in this field including anticancer therapies, drug delivery systems, and wound healing **(AL-Tameemi et al., 2025)**, gene delivery, biological sensing, and labeling technologies **(Elabbasy et al.,2025)**.

5.Green synthesis

There are three methods for the synthesis of nanoparticles, namely, physical, chemical and green synthesis **(Khan et al., 2023)**. Innumerable physical and chemical synthesis approaches require high radiation, highly toxic reductants, and stabilizing agents, which can cause pernicious effects to both humans **(Singh et al., 2018)**. As such, it is imperative to embrace environmentally friendly techniques that harness the power of natural **(Sani Aliero et al., 2025)**. Green synthesis method is the best method for the preparation of nanoparticles, and these methods are helpful to reduce the toxicity, increase the stability, eco-friendly, and cost-effective methods. Green synthesis methods have more beneficial response in environmental and biomedical applications **(Jeevanandam et al., 2022**). The green synthesis method can be defined as the nanoparticle synthesis process by using both biological materials and inorganic materials. The green synthesis method has many advantages over chemical and physical techniques, such cost-effectiveness, biocompatibility, and safety **(El-Khawaga et al., 2023).** Also,it is suitable for developing nanoparticles ranging from 1 to 100 nm compared to other related methods **(Vijayaram et al., 2023)**. Several scientific investigations have shown biological substrates to be the only possible raw materials for NP biosynthesis **(Al-darwesh et al., 2024)**. Therefore, the usage of stabilizers and reducing agents that possess a biological origin, such as microbial entities, fauna and various other resources, is a sustainable way to produce nano-sized materials **(Singh et al., 2023)**. Furthermore,many interesting biological methods using plants, algae, fungi, yeast, bacteria, viruses, etc., have been developed **(Soltys et al., 2021)**. Green-synthesized nanosized metal oxides exhibit enhanced reactivity owing to their organic capping molecules and crystalline imperfections, setting them apart from those produced chemically **(Abuzeid et al., 2023)**. Additionally, many studies have proved that zinc oxide nanoparticles (ZnONPs) made using green synthesis processes have strong antibacterial and photocatalytic properties (Sedefoglu, 2023). and have reported different biological activities **(Abbasi et al., 2020)**.

Second part

Experimental part

Chapter I

Materials and Methods

1.Materials

1.1. Chemicals, reagents and products

Zinc sulphate(**$ZnSO_4$**), chloroform , Tris (**$C_4H_{11}NO_3$**) ,Trichloroacetic Acid (**TCA**), Thiobarbituric Acid (**TBA**), Butylated Hydroxy Toluene (**BHT**),hydroxide de sodium(**NaOH**), Hydrogen chloride acid(**HCL**) , acid salicylique**($C_7H_6O_3$)**,dithio-bis-2-nitrobenzoic acid (**DTNB)** ,Riboflavin, phosphate buffer ,nitroblue tetrazolium (**NBT**), Bovine serum albumin (**BSA**) , Dipotassium phosphate (K2HPO4) , Potassium dihydrogen phosphate (**KH_2PO4**) ,Ethanol, Ethylene diaminetetraacetic acid (**EDTA**) , physiological solution (**Na Cl 0.9 %**) , distilled water .

All chemicals used in this study were purchased from Sigma-Aldrich Co (Alcobendas, Madrid, Spain) unless otherwise indicated.

1.2. Microorganisms

Gram-positive pathogenic bacteria such as *Staphylococcus aureus* DSM 1104 (*S. aureus*) were used. Gram-negative bacteria such as *Escherichia coli* LMG 8223 (*E. coli*) and *Klebsiella pneumonia* ATCC 43816 (*K. pneumonia*) were also used in this study. All the indicator bacteria were provided by the Laboratory of microbiology, Cellular and molecular Biology Department, Faculty of natural and life Sciences, El-Oued University, El-Oued, Algeria. They were stored in glass beads at −20 ◦C and subcultured into Brain Heart Infusion broth.

1.3. Animals and Breeding Conditions

Our study was conducted on twenty (26) male Wistar Albino rats aged 8 to 10 weeks and weighing between 150 and 218g. These animals were brought from the Pasteur Institute in Algeria and plastic cages lined with wood shavings bedding within the animal room of the Department of Molecular and Cellular Biology at the Faculty of Nature and Life Sciences, Echahid Hamma Lakhdar-El-Oued University, Algeria.The animals underwent a 10-day adaptation period under standard conditions of room temperature with a 12-hour light/dark cycle. Throughout the study, the rats were given free access to food and water.

1.3.1. Study design

After the adaptation period (10 days), the animals were divided equally into four groups of five rats each,as detailed below:

- **Group Control:** they were used, and they all received intraperitoneal injections of olive oil concurrently with the other groups.
- **Group CP:** They were injected with intraperitoneally with cisplatin (Platinol®) (5mg/kg).
- **Group CP+DF-ZnNPs:** were injected intraperitoneally with cisplatin (Platinol®): 5 mg/ Kg) + Intraperitoneal injection of DF-ZnNPs synthesized by dromedary Fat: 5 mg / Kg on the seventh day after cisplatin injection, after six day they were injected with the same dose of DF-ZnNPs.
- **Group CP+DF:**were injected intraperitoneally with cisplatin (Platinol®): 5 mg / Kg) + Intraperitoneal injection of Fat: 5 mg / Kg on the seventh day after cisplatin injection, after six day they were injected with the same dose of DF.

1.3.2. Sacrifice, blood sampling and Organ collection

Four days after treatment, the rats were sacrificed (by decapitation) following a 16-hour fasting period. under slight anesthesia by chloroform (94%). At the time of sacrifice, blood was collected in Heparin tubes and EDTA tubes for each rat. Blood glucose was measured by glucometer for each rat. After centrifugation at 3000 rpm for 15 minutes, serum and plasma were collected and stored at (-20°C). Serum was used for the determination of biochemical parameters (Blood sugar, Cholesterol, Creatine, TGO, TGP, Uric acid and Calcium), and the blood placed in tubes containing EDTA is used for the determination of hematological parameter.

After dissection, the liver, heart, kidneys and lungs tissues were carefully removed, rinsed with saline (Nacl 0.9%), and then weighed. A portion of organs (liver, kidneys and lungs) from each batch is fixed in 10% formaldehyde and kept in sample containers to produce histological study and stored at room. The organ homogenates were used to measure oxidative stress parameters (Reduced Glutathione (GSH), Malondialdehyde (MDA)and Super Oxide Dismutase (SOD)).

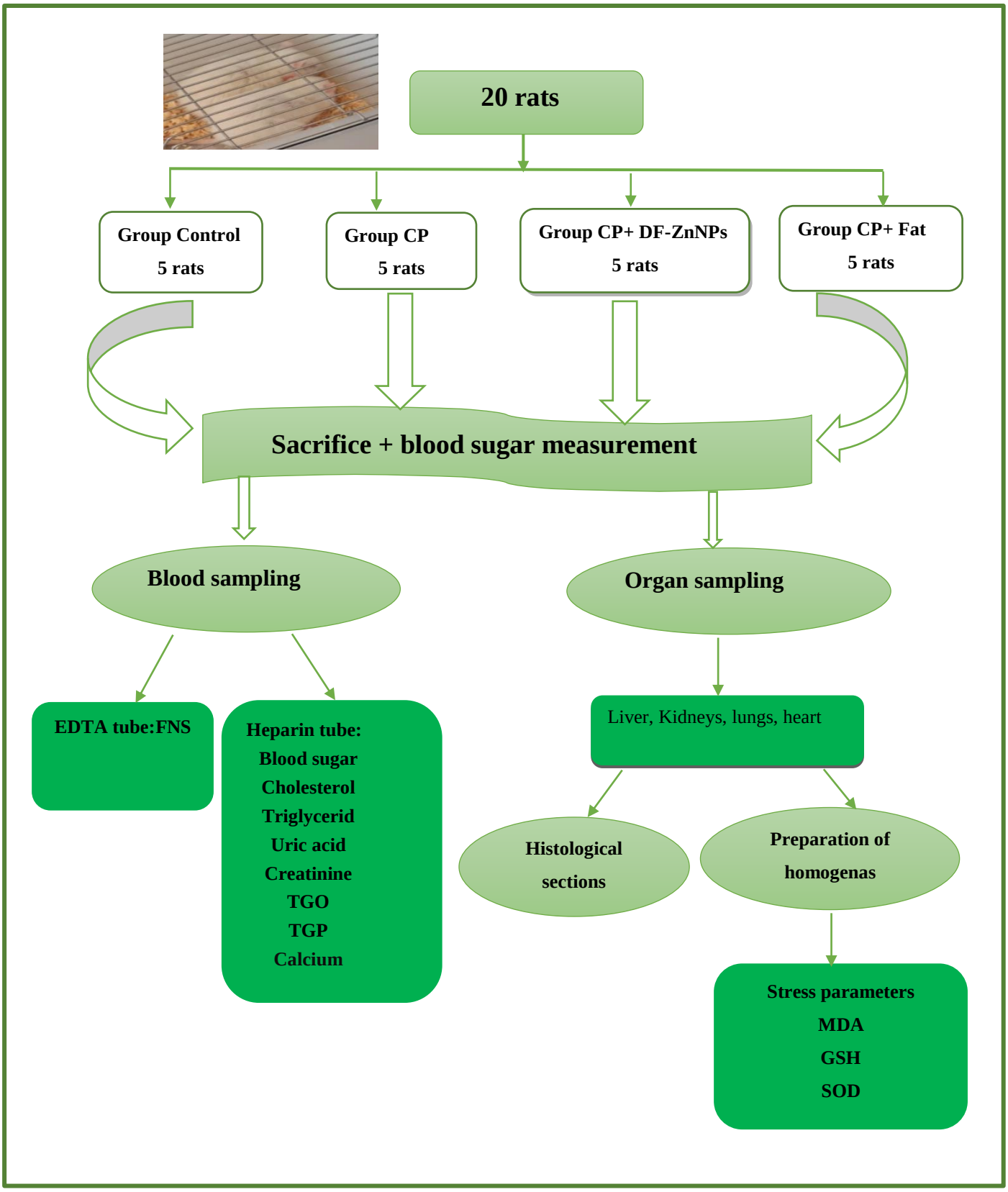

Figure 07: Experimental protocol of the study

2.Methods

2.1 *In vitro* study

2.1.1. Preparation of Fat dromedary's Oil

Following the slaughter of an adult male dromedary (from the hump), 2 kg of fresh fat were taken and promptly kept at -80°C. Approximately 500 grams of fat were thawed to room temperature for the trials. After that, each kind of defrosted fat was heated for 45 minutes to 60°C in a lab beaker. A food strainer (25 cm wire mesh sieve) was used to remove contaminants from each animal's crude melted fat. Each animal's clear liquid fat was then gathered in a sterile, clean container and kept in a refrigerator at 10°C until it was needed.

2.1.2. Synthesis of zinc oxide ZnO nanoparticles by dromedary Fat (DF-ZnNPs)

To make ZnNPs, 200 milliliters of aqueous zinc sulfate and 20 milliliters dromedary's Oil were combined. The zinc sulfate provided the ions that started the reaction, and the reaction mixture was constantly stirred in the dark at 60 degrees Celsius to prevent photo-catalysis. After 24 hours, the formation of ZnO NPs was indicated by an off-white color and then to gray-brown (figure08) . The final product was centrifuged (5000 rpm for 30 min), cleaned in ethanol and double-distilled water, respectively, dried, and stored in an amber sample bottle until it was needed **(chetehouna et al.,2024)**.

Figure 08: Steps of synthesis DF-ZnNPs

2.1.3. Characterization of DF-ZnNPs

A Perkins Elmer FTIR spectrometer (4000–400 cm−1) was used to identify the functional groups, using the KBr technique.UV-Vis spectrometer(UV- VIS) range of 200-600 nm to confirm the formation of nanoparticle.EDX analysis was used to determine the elementary calculation, while SEM (FESEM, JEOL-SEM, 6700F) was used to examine the surface morphology of the NPs. Image J software (Version IJ 1.46r) was used to compute the size distribution of nanoparticles using TEM pictures. Histograms are created from the measurements taken from the photos.

2.1.3.1. GC-MS analysis of DF-ZnNPs

1µl of dromedary fat was used to measure the volatile components using GC-MS analysis after the fat was produced in the universal solvent methanol. Headspace solid-phase micro-extraction (SPME) using DVB/CAR/PDMS fiber was employed to extract volatiles. First, the fiber was conditioned for four hours at 270°C in the GC injection port. After that, the fiber was placed in the vial containing the sample using an adapter and allowed to sit at room temperature for 15 minutes. The fiber was then inserted into a gas chromatograph's injection port for desorption. In the splitless mode, the desorption time was 10 minutes at 260°C. In order to conduct the analysis, a 7890A GC system (Agilent Technologies, Santa Clara, United States) was connected to a 5975C VL Triple-Axis mass detector. Helium was used as a carrier gas at a flow rate of 0.6 mL/min during the separation process on a DB-5MS capillary column (25 m × 0.2 mm; 0.33 µm film thickness; J&W, Folsom, California). The injector and transfer line had respective temperatures of 260°C and 280°C. The wavelength-range scanned was 275– 350 nm using Sykam S3240 UV multichannel detector.

2.1.3.2.X-ray diffraction of DF-ZnNPs

An X-ray diffractometer (PROTO® AXRD Benchtop) was utilized to detect the chemical formula, crystallite structure, lattice parameters and crystallite size of ZnO NPs. The XRD was performed in the scaling angle (2θ) range of 10-80° with Cu Kα radiation (λ = 1.540593 Å). The crystallite size was determined using the Debye-Scherrer equation, which is written as $D = k \lambda/\beta \cos \theta$. The Scherrer constant (0.9-1), the X ray wavelength (1.540593 Å), the full-width half maximum (FWHM), and the Bragg angle (θ), both stated in radians, are the parameters that are

taken into consideration by the formula. Using formula 1/(d2) = (3/4) [(h2+hk+k2)/a2] +(l2/c2), where d is the interplanar spacing and h, k, and l are the Miller indices, the lattice parameters a, b, and c were found.

2.1.4. Antibacterial activity

The Antibacterial activity was carried out using disc diffusion method. The disc diffusion assay on Mueller Hinton agar plates against common Gram-negative (*Klebsiella pneumoniae and Escherichia coli*) and Gram-positive (*Staphylococcus aureus*) bacteria was performed to evaluate the antibacterial properties of DF-ZnNPs prepared in DMSO. Bacteria were conserved on nutrient agar plates at 4°C. Activation of bacteria was performed at 37°C in the incubator, overnight. The bacterial suspension was prepared in sterile physiological water. The suspension was spread uniformly on the dried surface of Muller Hinton agar by streaking. After that, sterile paper discs (Whatman No. 3) of 6 mm were impregnated with 20 µL of DF-ZnNPs solutions (40 mg/mL), and discs were than dried in a clean bench before were placed on the inoculated agar surface. Discs impregnated with preparation solvents (DMSO) were used as control. The all plate was incubated at 37°C for 24 h. Ampicililn and chloramphenicol were used as standards against all pathogens. After incubation, the zone of inhibition around each disc was measured in millimeters unit **(chethouna et al.,2023)**.

2.2. *In-vivo* study

2.2.1. Acute toxicity evaluation

for acute toxicity evaluation Lorke's method was used **(Lork ,2023)** with some modifications, to test the DF-ZnNPs. Six rats were maintained fasting for 12 h, each rat was injected intraperitoneally with a single dose of DF-ZnNPs (Control, 25 and 50 mg/Kg body weight). The rats were kept under observation for a full day in order to track both their mortality and behavior. The rats were placed under observation for 20 days after.

2.2.2. Hematological analysis

Hematological parameters were determined an automated "MINDRAY-BC30 "analyzer. It performs a quantitative and qualitative electronic analysis of the blood's constituent elements: white blood cells (WBC), lymphocytes, granulocytes, red blood cells count (RBC), hematocrit level (HCT), hemoglobin level (HGB), mean Corpuscular Hemoglobin (MCH), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), Platelets (PLT).

2.2.3. Biochemical analysis

Biochemical analysis by"MINDRAY BA- 88 A". The metrics included blood sugar cholesterol, triglyceride, creatinine, TGO, TGP, uric acid, calcium.

2.2.4. Oxidative stress parameters

2.2.4.1. Homogenates preparation

0.5 gram of tissues (liver, heart, lungs, and kidney) from each rat in the different study groups was used. After grinding and homogenizing the tissues in in 5 ml of phosphate buffer solution (PBS, pH = 7.4). Homogenates were centrifuged at 5000 rpm for 15 min. and the supernatant was then stored at -20°C until the oxidative stress parameter assays were performed.

2.2.4.2. Determination of Malondialdehyde (MDA) level

- **Principle**

The common method for the assessment of MDA level is the thiobarbituric acid (TBA) assay, where MDA forms a complex with two molecules of 2-thiobarbituric acid (TBA) in the presence of acidic medium and heat. A change in the color of the solution to a pink color is an indication of the presence of MDA **(Yagi, 1976)**.

- **Reagent**

375mg of TBA, 20g of TCA, 0.01g of BHT, 25ml of 1N HCL and 50ml of distilled water were introduced into a beaker. The solution obtained was heated to 40° C. in a water bath until the TBA was completely dissolved, then transferred to a 100 ml flask and the volume filled up with distilled water to the gauge**.**

❖ **Procedure**

Pipeter dans les tubes à essai en verre et à vis, 200µl d'échantillon, 800 µl de réactif TBA et fermer hermétiquement. Chauffer le mélange au bain Marie à 100°C pendant 15 minutes. Puis refroidir dans un bain d'eau froide pendant 30 minutes en laissant les tubes ouverts pour permettre l'évacuation des gaz formes lors de la réaction. Centrifuger à 3000 tours/minutes pendant 5 minutes et lire l'absorbance du surnageant à 532 nm à l'aide d'un spectrophotomètre.

❖ **Expression of results**

The concentration of TBARS was determined using the molecular extinction coefficient of MDAThe (å= 1.53 105 M-1 cm-1) results were expressed in µmol/mg.

MDA (µmol/mg of prot) = (OD sample /1.53 x 10^5) / mg of protein

2.2.4.3. Determination of reduced glutathione (GSH) level

❖ **Principal**

In our study, glutathione was determined using a colorimetric method **(Weckbecker &CORY, 1988)** By measuring the optical density results from the formation of 2-nitro-5-mercapturic acid (TNB) from the reduction of dithio-bis-2-nitrobenzoic acid (DTNB)which is called Ellman's reagent, with the SH groups present in GSH**.**

❖ **Procedure**

1.800 µl of homogenate samples are added to 200 µl of salicylic acid (0.25%). Then centrifuged at 1000 rpm for 5 min.

2.Let the mixture stand for 15 minutes in the refrigerator. Then centrifuged at 1000 rpm for 5 min.

3.Take 500 ml of supernatant and mix it with 1000 µl of tris buffer solution (tris 0.4 mol, NaCl 0.02 mol; ph = 8.9) and 25 µl of DTNB (0.01 mol/L).

4. Incubate the mixture for 5 minutes at room temperature and measure the absorbance at λ = 412 nm using a spectrophotometer.

❖ **Expression of results**

The concentration of GSH expressed in nanomoles per milligram of protein (nmol/mg prot) is calculated according to the following formula:

$$GSH(nM/Mg\ de\ prot) = \frac{DO \times 1 \times 1.525}{13133 \times 0.8 \times 0.5 \times mg\ de\ prot} \times$$

OD: Optical Density**.**

1.525: total volume of blend an ml.

13133: Absorption constant of SH groups at 412 nm.

0.5: volume of solution float an ml.

1: volume of protein mixture.

0.8: volume of homogeneous solution without protein exists in 1 ml.

GSH: concentration of glutathione.

d: dilution factor.

2.2.4.4. Determination of Super Oxide Dismutase (SOD) activity

❖ **Principle**

In our study, the enzymatic activity of Super Oxide Dismutase (SOD) was measured by the method of **(Beauchamp &Fridovich.,1971)**. This method is based on the the inhibition of NBT reduction by SOD. NBT is reduced by the superoxide anion O2-, and it is known that SOD neutralizes O2-, which inhibits the reduction of NBT.

❖ **Procedure**

Collect in tubes	Blank	Sample
EDTA-Met (0.1mM, 13mM)	1000µL	1000µL
Phosphate buffer (50Mm)	892,2µL	892,2µL
Sample	-	50
Phosphate buffer (50Mm)	1000µL	950µl
NBT (75µM)	85,2µL	85,2µL
Riboflavin (2µM)	22,6µL	22,6µL

❖ **Expression of results**

Inhibition percentage of NBT reduction by SOD as follows**:**

IP (%) = (OD blank–OD sample)/ (OD blank) ×100

2.2.5. Histopathological study

After fixing portions of the liver, kidneys, and lungs in formaldehyde for at least 24 hours, the samples were processed using the tissue processor "SLEE MTP" for 16 hours. This involved passing through twelve containers, beginning with ethanol, followed by xylene, and ending with paraffin. Subsequently, the inclusion (embedding) process was carried out, and tissue sections with a thickness of 3 micrometers were obtained using a microtome. The paraffin was removed by immersing the sections in a water bath at 45°C, after which the samples were placed in an oven at 60°C. Once dried, the slides were stained in successive Deparaffinization for 15 minutes, hydration to remove xylene and replace with water, alcohol (ethanol) for 2 minutes + alcohol (2 minutes), and alcohol (2 minutes), followed by washing with tap water (1 minute).

hematoxylin staining for 1 minute after washing (1 minute) and then eosin staining (1.5 minutes). stages and examined under a microscope (OPTIKA).

2.2.6. Statistical Analyses

Statistical evaluation was performed using the Student's T test. The results were expressed as the mean plus or minus standard error of the mean [Mean± SEM].

We then use MINITAB 13.0 software and EXCEL software to help us perform the tests Differences were considered:

- ✓ Non-significant ($P > 0.05$).
- ✓ Significant when ($*P < 0.05$).
- ✓ Highly significant when compared to the control ($**P < 0.01$).
- ✓ Very highly significant when compared to the control ($***P < 0.001$).
- ✓ With P: Significance threshold

Chapter II

Results

1.*In vitro* study

1.1. Characterization of DF-ZnNPs

1.1.1. UV-VIS spectroscopy

The optical properties of DF-ZnNPs were characterized using UV-Vis spectroscopy,as shown in **(Figure 09)**. The was production of DF-ZnNPs further confirmed by the lightabsorption patterns at regular intervals in the range of 200 to 400 nm, and a prominent absorption peak was observed at 300 nm.

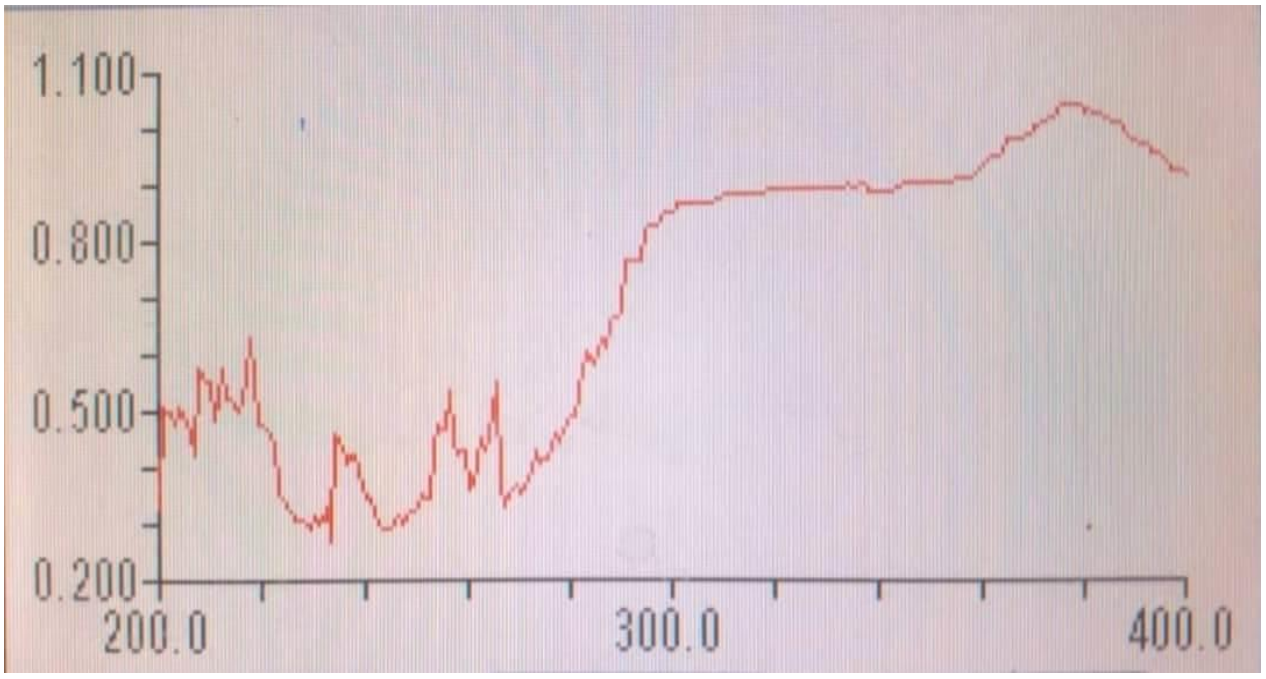

Figure09: UV-Visspectrumof DF-ZnNPs

1.1.2. FTIR analysis

FTIR analysis showed a broad peak in the 3400 cm^{-1} showed the O-H (hydroxyl group) stretching bond vibration present in alcohols or carboxylic acids, 2900-2800 cm^{-1} region we see some peaks in the carbon-hydrogen stretching region, which may indicate the presence of aliphatic chains (consistent with the "fat" component). Also shown is a small and rather undefined peak in the range 1700-1600 cm- this is a stretch of the carbonyl C=O, of a fatty acid, the region 1400-1000 cm-1 shows several peaks, these peaks may be due to vibrations of C-O (ether group) or C-N (amine group). Also, several peaks appear in the region below 1000 cm-1000 cm-1. These peaks are due to vibrations of Zn-O (zinc oxide) as well as the "fingerprint" of the molecule. While the peak at 500 cm^{-1} was attributed and make sure to the Zn-O stretching vibration.

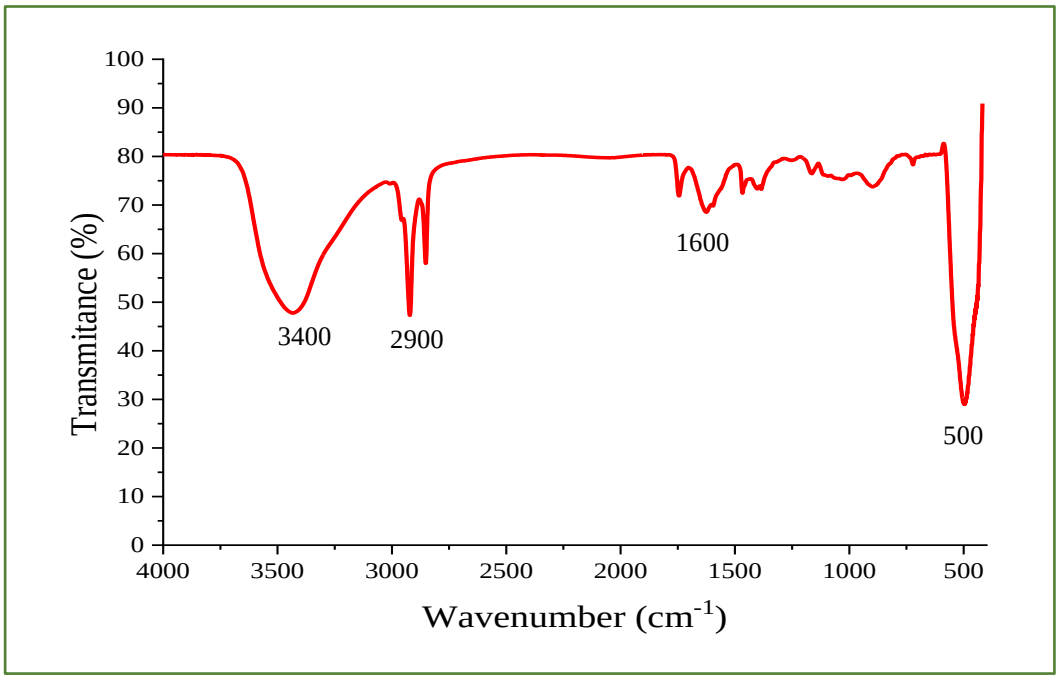

Figure 10: FTIR spectrum of DF-ZnNPs

1.1.3. Scanning electron microscopy and EDX

SEM analysis showed that the DF-ZnNPs is somewhat agglomerated structure zoom on x60;000 and x150,000 **(Figure 11)** magnification, which is extremely high. The particles appear to be somewhat spherical, but they are clumped together. EDX analysis obtained peak band in the range of 1-2 KeV, presented strongest signal from zinc region and weaker signal from O atom which indicates the presence of elemental zin oxide in the nanoparticle. zinc as the major constituent element (72%) and oxygen (27%) (**Figure 12)**.

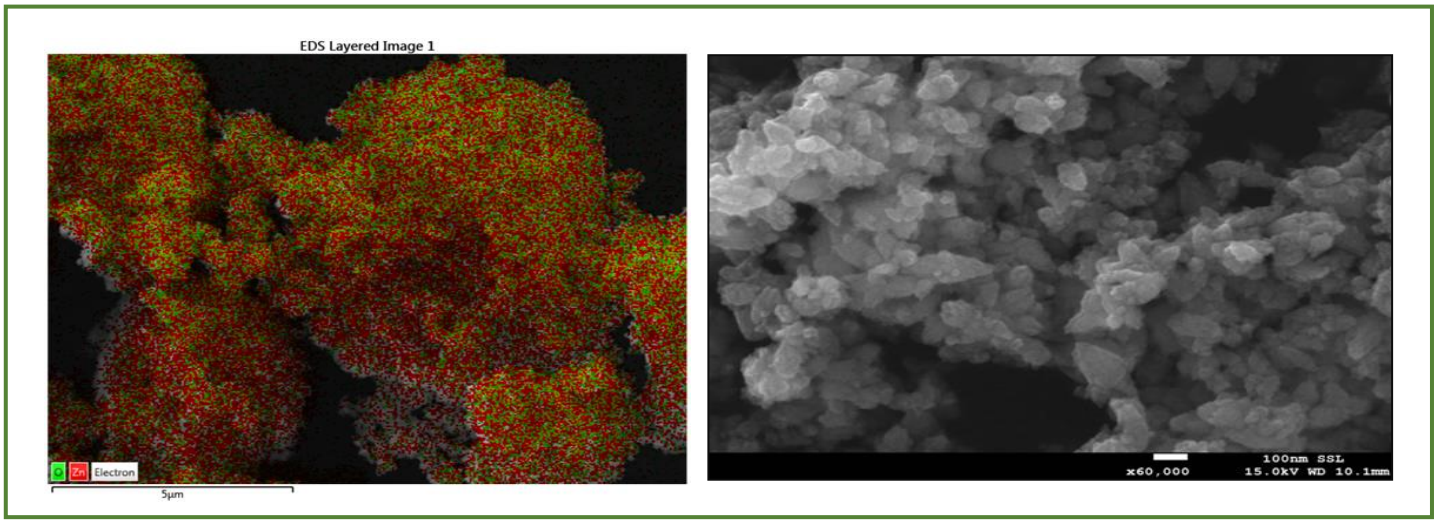

Figure11: SEM image of DF-ZnNPs

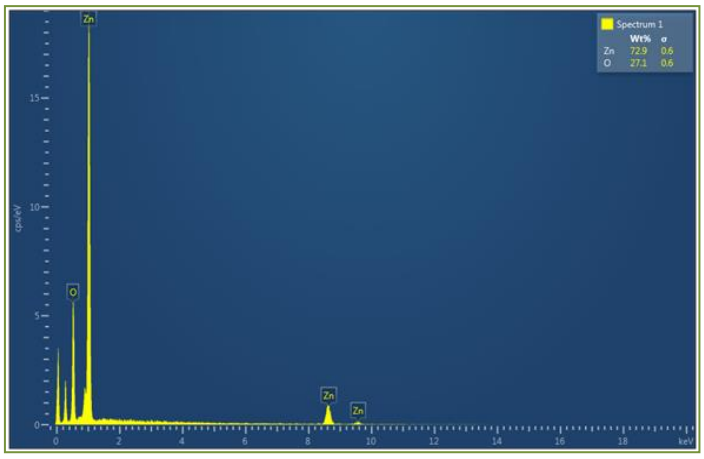

Figure 12: EDx Spectroscopy of DF-ZnNPs

1.1.4.TEM image

Transmission electron microscopy (TEM) analysis confirms the formation of DF-ZnNPs and provides single images of DF-ZnNPs synthesized at 10 nm scales **(figure 13 C)**. We observe a relatively uniform distribution of roughly spherical or slightly irregular nanoparticles. The histogram provides a more accurate description of the particle size distribution (figure 13 D). The reported average particle size is 2.67±0.96 nm. The standard deviation of 0.96 nm indicates a moderate degree of size variation within the sample. Although not completely homogeneous, the particles are reasonably close to the average in size.

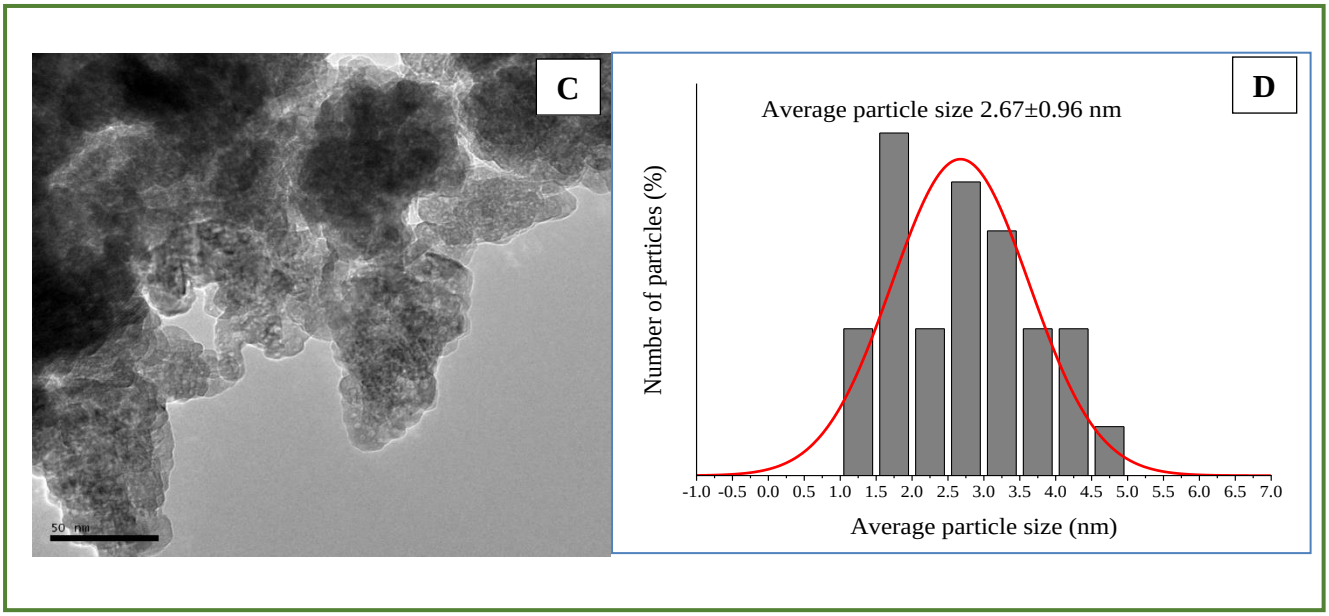

Figure 13: TEM image(C) and Average particule size (D) of DF-ZnNPs

1.1.5. Fatty acids GC-MS Analysis of DF-ZnNPs

The screening and the identification of fatty acids compounds of that coate Zinc nanoparticles were conducted through GC-MS chromatogram **(Figure 14 and 15figure)**. Using the GC-MS technique, more than 5 components were identified. The chemical constituents of DF-ZnNPs were pentadecanoic acid methylester, Benzoic acid-methylester, Tetradecanoic Acid 12 methyl- methyl ester, stearic acid methyl ester, cic-10-heptadecanoic acid-methyl ester, 9,12-Octadecadienoic acid (Z,Z).

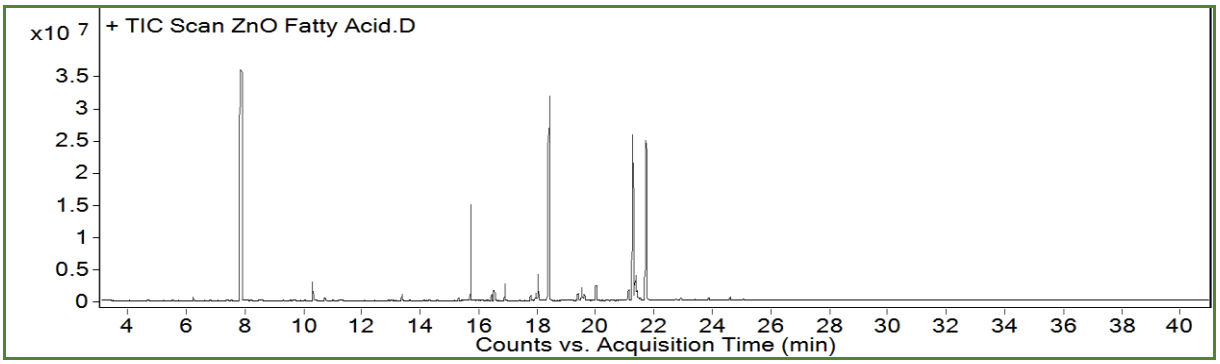

Figure14: Fatty acids Chromatogram of DF-ZnNPs

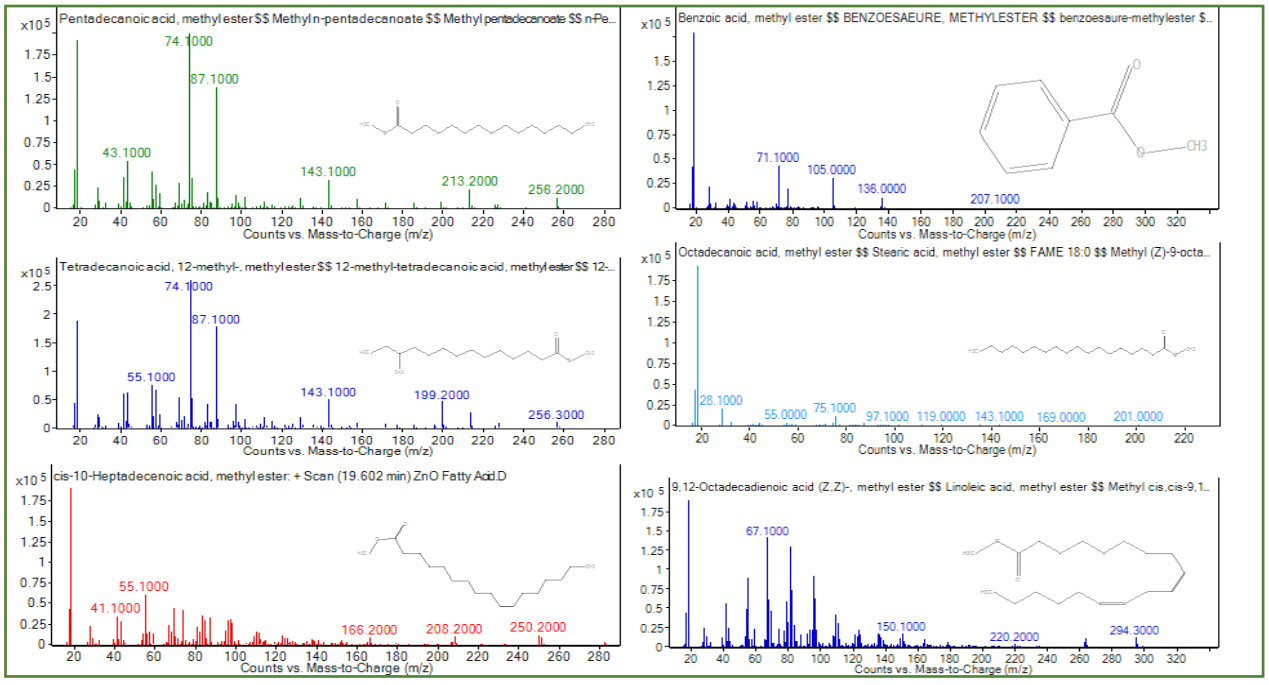

Figure15: Mass Spectrometry of DF-ZnNPs

1.1.6.X-ray diffraction of DF-ZnNPs

According to the XRD data that matched the JCPDS card Nº 01-079-0205 database, the chemical formula of the zinc oxide nanoparticles was ZnO, and their crystallite structure was hexagonal. The lattice parameters were a = b = 2.43 Å ≠ c = 3.67 Å, with a crystallite size (D) of 22.0 nm. The diffraction angles corresponded to the (100), (002), (101), (102), (110), (103), and (112) h, k, and l crystallite planes, respectively, with peaks at 31.97°, 34.60°, 36.47°, 47.79°, 56.80°, 63.03°, 68.11° **(Figure16)** .

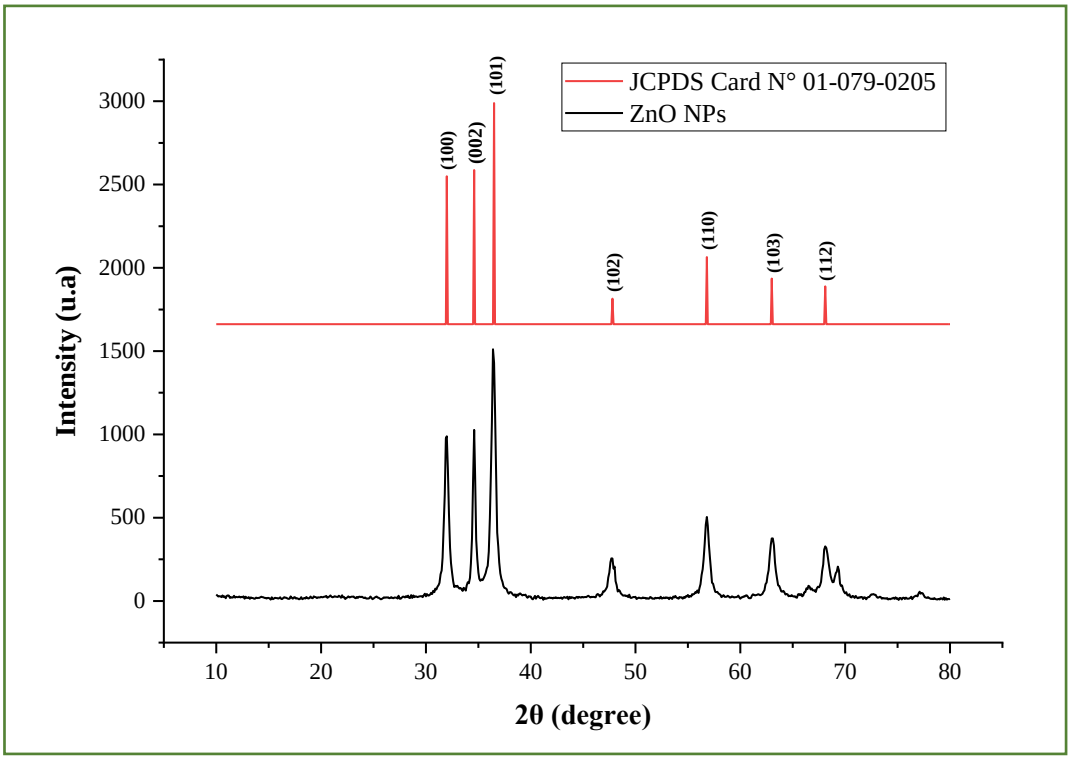

Figure16: XRD patterns of DF-ZnNPs.

1.2. Antibacterial activity of DF-ZnNPs

In general, the DF-ZnNPs demonstrated a clear inhibitory activity against E. coli **(Table 1 and Figures 17)**, where the inhibition zone reached 12.5 mm, while the inhibition zone of pure fat was only 6.2 mm **(Table1 and Figure 17(A-C))**. This indicates that the addition of zinc oxide to the fat significantly enhanced its antimicrobial activity against *E. coli*. Though the DF-ZnNPs showed inhibitory activity against *Staphylococcus aureus*, with an inhibition zone of 11 mm. As for, pure lipids did not show any inhibitory activity against these bacteria. Interestingly, ampicillin showed much stronger activity against these bacteria (39 mm), while chloramphenicol was similar to DF-ZnNPs (19 mm). This is the last one, showed good inhibitory activity with an inhibition zone of 10.5 mm against *klebsiella pneumonia*, and 7.4 mm for pure fat compared to ampicillin. However, chloramphenicol is more effective against these bacteria.

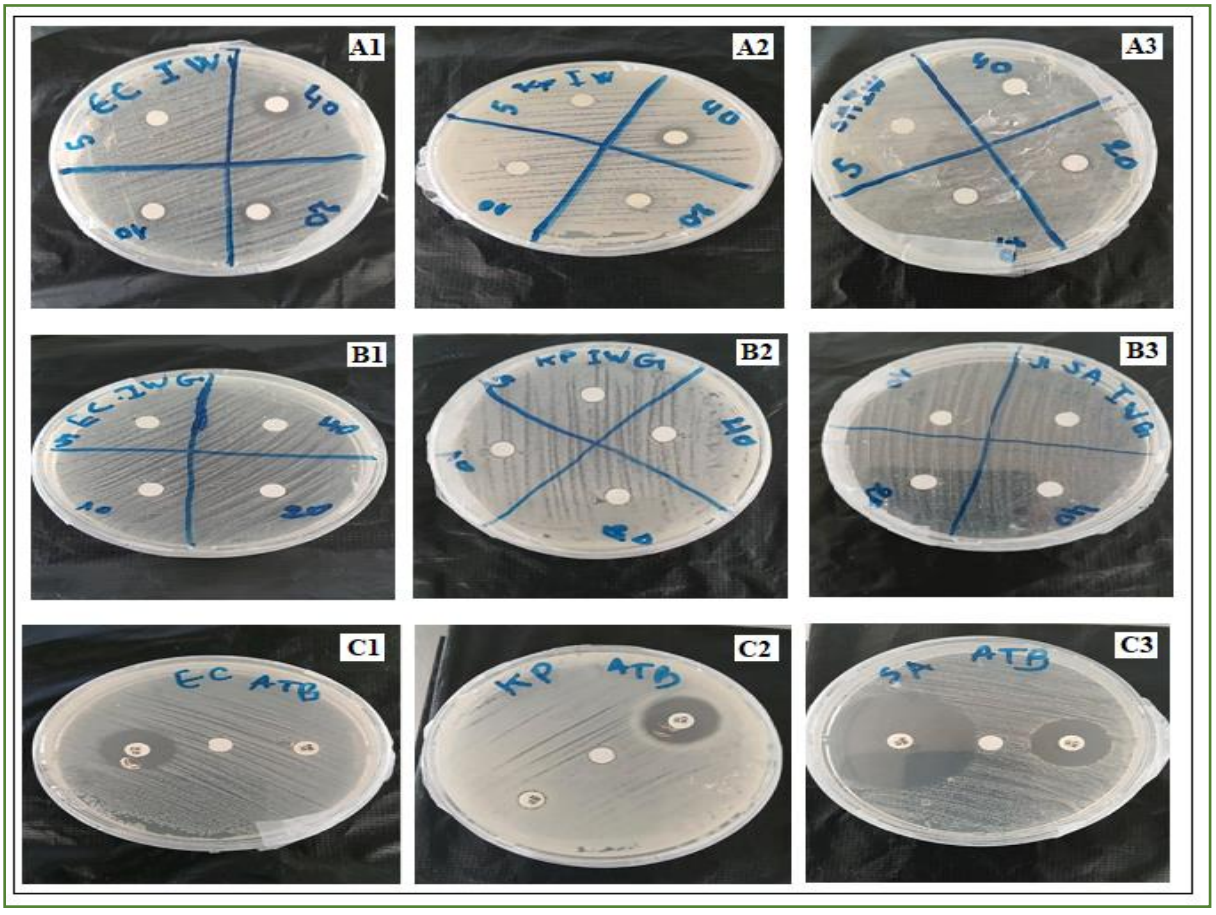

Figure 17: Showing Zone of Inhibitions produced by DF-ZnNPs (A1-A3), DF (B1-B3) and Antibiotic (C1-C3) against different bacterial strains tested.

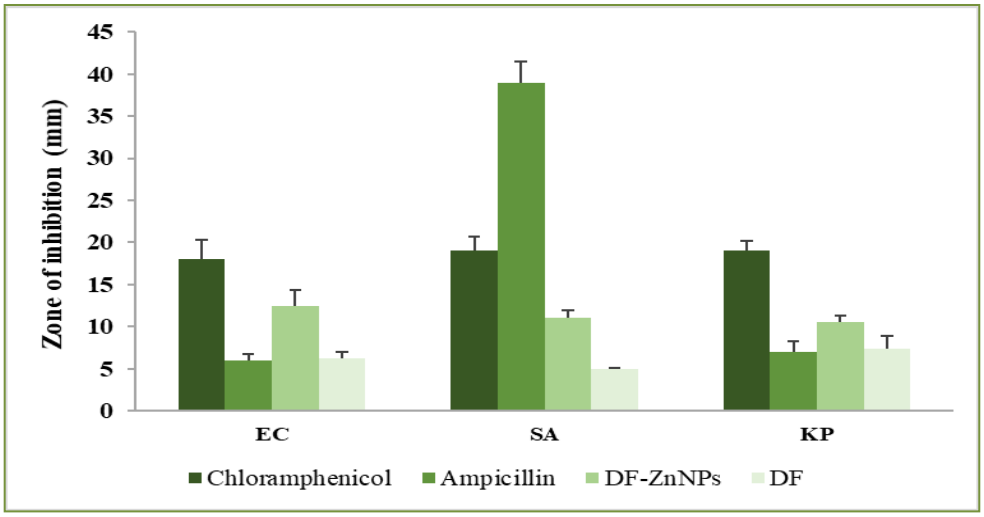

Figure 18: Antibacterial activity of biosynthesized DF-ZnNPs

2.*In-vivo* study

2.1. Acute toxicity evaluation

No mortality was noted on the acute toxicity test at any DF-ZnNPs dose tested. No symptoms of toxicity effects on behavioral and physiological parameters, including skin, eyes, diarrhea, and sleep were recorded during this period. All animals administered with any dose tested showed no signs of toxicity, their behavioral and physiological parameters were normal, and no mortality was recorded during the 21 days of the experimental period **(Table 02)**.

Table 01: Mortality, physiological parameters and behaviour observations after acute toxicity using zinc oxide nanoparticles

Parameter	Dose	Toxicity time									
		0 h	**0.5 h**	**3 h**	**6 h**	**12 h**	**18 h**	**1 d**	**7 d**	**14 d**	**21 d**
Mortality	**Control**	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
	25 mg/ kg	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
	50 mg/ kg	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
Skin	**Control**	/	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)
	25 mg/ kg	/	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)
	50 mg/ kg	/	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)
Eyes	**Control**	/	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)
	25 mg/ kg	/	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)
	50 mg/ kg	/	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)
Diarrhea	**Control**	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
	25 mg/ kg	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
	50 mg/ kg	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
Sleep	**Control**	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
	25 mg/ kg	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
	50 mg/ kg	/	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %

(n): normal / 0 %: none

2.2. Relative organ weight of rats

The results obtained show an increase in the relative weight of all organs in group CP, significantly ($p < 0.05$) in the kidneys, not significantly ($p > 0.05$) in the lungs, and very highly significantly ($p < 0.001$) in the heart and liver of group CP compared to the control group. However, the relative weight of liver and kidney decreased very highly significantly ($p < 0.001$), that of heart and lung decreased significantly and non-significantly ($p < 0.05$, $p > 0.05$) respectively in the CP+DF-ZnNPs treated group compared to the CP group. As for the CP+DF treated group, there was no significant difference ($p > 0.05$) in the relative weight of all organs compared to the CP group.

Table 02: Relative weight of organs (liver, heart, kidneys, and lungs) of the different experimental groups

Relative weight(g)	Control (n=5)	CP (n=5)	CP+DF-ZnNPs (n=5)	CP+DF (n=5)
Liver %	2.8293±0.0147	3.2227±0.0328***	2.8250±0.0716$^{NS, c}$	3.0303±0.0947$^{NS, NS}$
Heart %	0.3130 ±0.0023	0.3250±0.00167***	0.31467±0.0041$^{NS, a}$	0.31700±0.0058$^{NS, NS}$
Kidneys %	0.56833±0.0082	0.6523±0.0231*	0.6000±0.0022$^{***, c}$	0.6320±0.0424$^{NS, NS}$
Lungs %	0.8790±0.0057	1.1485±0.0921^{NS}	1.0375±0.0944$^{NS, NS}$	1.0427±0.0804$^{NS, NS}$

Comparison with control group: * p < 0.05; p** < 0.01, p*** < 0.001, with CP control group: p^{a}< 0.05, p^{b}< 0.01, p^{c}< 0.001, n = 5 rats.P: significance level

2.3. Hematological parameters

The results of the hematological analysis of the experimental showed a very highly significant increase (p < 0.001) in all white blood cell (WBC) parameters for group CP compared to the control group. Compared to group CP, there was a significant decrease (p < 0.05) in white blood cells, a non-significant decrease (p > 0.05) in lymphocytes, and a very highly significant decrease (p < 0.001) in granulocytes in group CP+DF-ZnNPs compared to group CP. In group CP+DF, there was a highly significant decrease (p < 0.01) in granulocytes, a very highly significant decrease (p < 0.001) in white blood cells, and a non-significant decrease (p > 0.05) in lymphocytes**.**

Table 03: Leukocyte line in blood of control and experimental groups

Parameter	Control (n=5)	CP (n=5)	CP+DF-ZnNPs (n=5)	CP+DF (n=5)
WBC (10^9/L)	7.200±0.462	9.867±0.394***	7.900±0.634$^{NS, a}$	7.1333±0.0919$^{NS, c}$
lymphocytes (10^9/L)	5.633±0.373	7.200±0.193***	4.697±0.423$^{NS, NS}$	4.700±0.352$^{*, NS}$
granulocytes (10^9/L)	1.467±0.117	2.6500±0.0671***	1.733±0.117$^{NS, c}$	1.467±0.214$^{NS, b}$

Comparison with control group: * p < 0.05, p*** < 0.001, with CP control group: p^{a}< 0.05; p^{b}< 0.01, p^{c}< 0.001, n = 5 rats.P: significance level.

The results obtained compared to the control group show a highly significant decrease ($p<0.01$) in red blood cells (RBC) to a very highly significant decrease ($p<0.001$) in hemoglobin (HBG), hematocrit (HCT), a non-significant decrease ($p>0.05$) in MCHC, with a significant increase ($p<0.01$) in PLT and MCH to a highly significant increase ($p<0.01$) in MCV for the CP group compared to the control group. Conversely, RBC and HCT increased highly significantly ($p < 0.01$) and non-significantly ($p > 0.05$) in HGB and MCHC, while there was a very highly significant ($p < 0.001$) decrease in MCV and MCH and non-significantly ($p > 0.05$) in PLT in group CP+DF-ZnNPs compared to group CP. Moreover, in group CP+DF, we observed a highly significant ($p < 0.01$) increase in HCT at a very highly significant increase ($p < 0.001$) in RBC and HGB, while there was a highly significant ($p < 0.01$) decrease in MCV and MCH at a very highly significant ($p < 0.001$) decrease in PLT, with a non-significant ($p > 0.05$) decrease in MCHC compared to group CP.

Table 04 : Erythrocyte and Platelet line in blood of control and experimental groups

Parameter	Control (n=5)	CP (n=5)	CP+DF-ZnNPs (n=5)	CP+DF (n=5)
RBC (10^12/L)	7.110±0.138	5.870±0.257**	7.893±0.372$^{NS,\ b}$	6.9433±0.0626$^{*,\ c}$
HGB (g/dL)	14.150±0.307	12.267±0.243***	14.450±0.887$^{NS,\ NS}$	13.533±0.138$^{**,\ c}$
HCT%	40.40±1.09	34.767±0.810***	40.88±1.58$^{NS,\ b}$	38.100±0.891$^{NS,\ b}$
MCV (FL)	57.367±0.390	61.425±0.125***	53.233±0.366$^{***,\ c}$	56.883±0.752$^{NS,\ b}$
MCH (Pg)	20.300±0.238	21.700±0.231**	18.767±0.256$^{***,\ c}$	19.533±0.387$^{NS,\ b}$
MCHC (g/dL)	35.075±0.287	34.925±0.450^{NS}	35.375±0.466$^{NS,\ NS}$	34.200±0.297$^{NS,\ NS}$
PLT (10^9/L)	906.0±14.3	1141.8±26.2**	1059±171$^{NS,\ NS}$	913.5±11.3$^{NS,\ c}$

Comparison with control group: * $p < 0.05$; $p^{**} < 0.01$, $p^{***} < 0.001$, with CP control group: $p^{b} < 0.01$, $p^{c} < 0.001$, n = 5 rats.P: significance level.

2.4. Biochemical parameters

Regarding biochemical parameters, tests were performed for uric acid, creatine, cholesterol, triglycerides, blood glucose, and calcium, in addition to the following enzymatic tests: TGO and TGP. To support the results.

Our results showed a highly significant increase ($p<0.01$) in blood sugar levels observed in the CP group compared to the control group. While blood sugar levels decreased significantly in the CP+DF-ZnNPs group ($p<0.05$), and non-significantly ($p>0.05$) in the CP+DF group compared to the CP group. As for cholesterol results, they showed a highly significant increase ($p<0.01$) in the CP group compared to the control group. Cholesterol levels also decreasedhighly significantly ($p<0.01$) and non-significantly ($p>0.05$) in the CP+DF-ZnNPs and CP+DF groups compared to the CP group. Furthermore, the results we obtained for triglycerides showed a highly significant increase ($p<0.01$) compared to the control group**.** In contrast**,** we observed a highly significant decrease in triglycerides ($p<0.001$) in both the CP+DF-ZnNPs and CP+DF groups compared to the CP group. The results showed a significant increase ($p<0.05$) in creatine levels in the CP group compared to the control group. However, creatine levels decreased non-significantly ($p>0.05$) in the CP+DF-ZnNPs and CP+DF groups, respectively, compared to the CP group. Uric acid levels showed a highly significant decrease ($p<0.01$) in the CP group compared to the control group. While they increased significantly ($p<0.05$) in group CP+DF-ZnNPs, and decreased non-significantly ($p>0.05$) in group CP+DF, in the same analysis compared to group CP. Regarding the results of serum TGO and TGP activities, there is a significant increase ($p<0.05$) in serum TGO activity and a highly significant increase ($p<0.01$) in serum TGP activity in group CP compared to the control group. On the contrary, the activity of the TGO decreased highly significantly ($p<0.01$) in the CP+DF-ZnNPs group and very highly significantly ($p<0.001$) in the CP+DF group, while the serum activity of TGP decreased significantly ($p<0.001$) in the CP+DF-ZnNPs and CP+DF groups compared to the CP group. We also observed in calcium levels a non-significant increase ($p>0.05$) in the CP group compared to the control group, while the calcium levels decreased highly significantly ($p<0.01$) in the CP+DF-ZnNPs group and very highly significantly ($p<0.001$) in the CP+DF group compared to the CP group.

Table05: Serum Concentration of Blood sugar, Cholesterol,Creatine, Transaminase Activity (TGO, TGP),Uric acid and Calcium of control and experimental groups.

parameters	Control (n=5)	CP (n=5)	CP+DF-ZnNPs (n=5)	CP+DF (n=5)
Blood sugar(g/l)	0.8800±0.0228	1.2150±0.0318**	1.0100±0.0518$^{NS, a}$	1.1167±0.0528$^{**, NS}$
Cholesterol(g/l)	0.6666±0.00919	0.9833±0.0712**	0.7433±0.0538$^{NS, b}$	0.8933±0.0639$^{*, NS}$
Triglycerides(g/l)	0.4200±0.0096	0.8050±0.0433**	0.5033±0.0264$^{*, c}$	0.5333±0.0410$^{*, c}$
Creatine(mg/l)	8.690±0.123	10.167±0.628*	10.065±0.326$^{**, NS}$	9.810±0.110$^{***, NS}$
TGO(UI/I)	100.05±0.20	159.6±11.2*	128.25±4.47$^{**, b}$	113.41±1.26$^{**, c}$
TGP(UI/I)	27.123±0.638	50.11±2.22**	32.15±2.69$^{NS, c}$	28.670±0.340$^{*, c}$
Uric acid(mg/l)	20.715±0.078	17.007±0.729**	24.35±1.94$^{NS, a}$	15.713±0.529$^{***, NS}$
Calcium(mg/dl)	8.297±0.371	10.168±0.652 ^{NS}	8.030±0.412$^{NS, b}$	8.6233±0.0649$^{**, c}$

Comparison with control group: * $p < 0.05$; $p^{**} < 0.01$, $p*** < 0.001$, with CP control group: $p^{a} < 0.05$; $p^{b} < 0.01$, $p^{c} < 0.001$, n = 5 rats. P: significance level

2.5. Evaluation oxidative stress parameters

2.5.1. Tissue Malondialdehyde (MDA) Concentrations

Our results showed a highly significant increase ($p<0.01$) in tissue Malondialdehyde (MDA) concentration in the liver and lungs, and a non-significant increase ($p<0.05$) in the heart and kidney of the CP group compared with the control group. Compared with the CP group, the MDA concentration increased highly significantly ($p<0.01$) in the kidney and decreased non-significantly ($p>0.05$) in the liver, heart and lungs of the CP+DF-ZnNPs treated group. As for the CP+DF treated group, no significant variation ($p>0.05$) was observed in any organs. Except for the liver, the MDA concentration increased non-significantly ($p>0.05$) and decreased non-significantly ($p>0.05$) in the lungs.

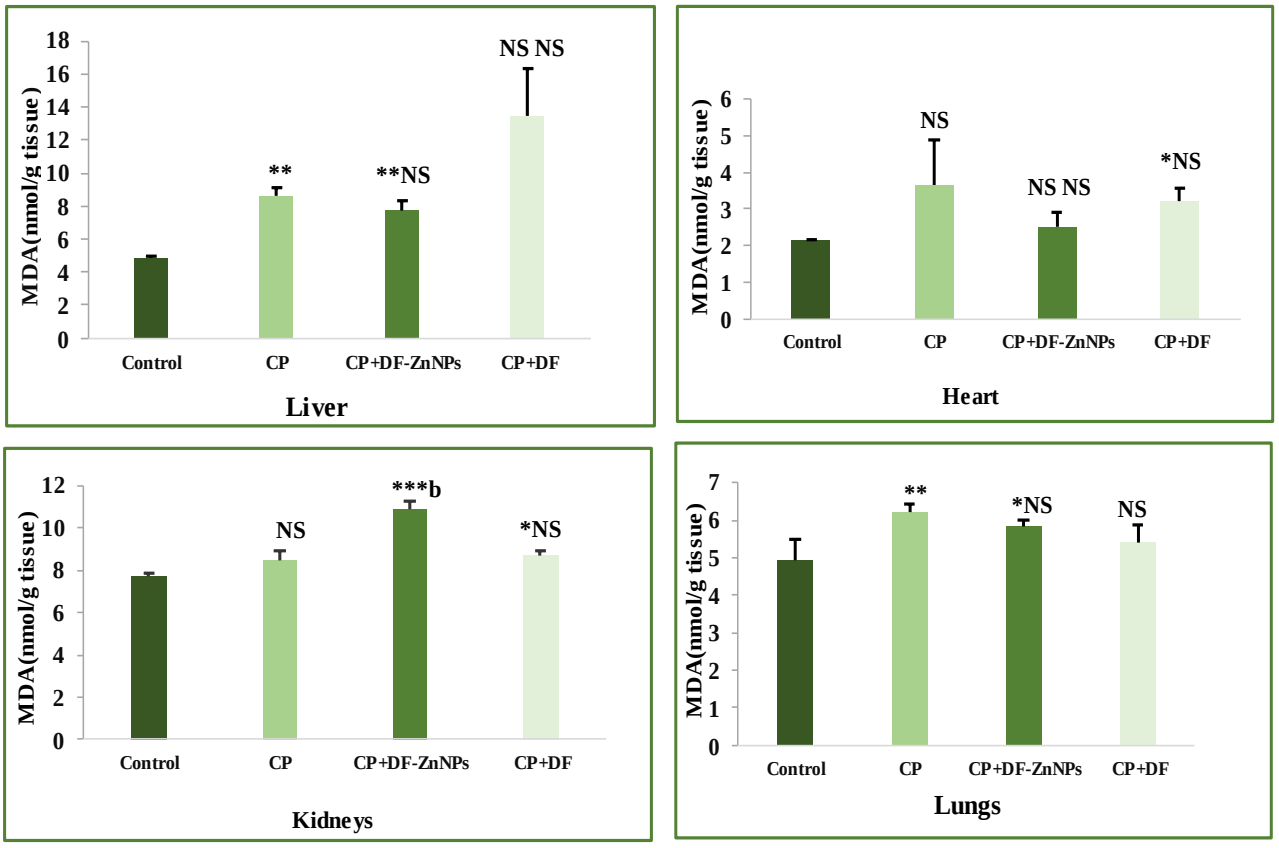

Figure 19: Tissues MDA Concentrations in control and experimental groups

Comparison with control group: * $p < 0.05$, $p^{**} < 0.01$, $p^{***} < 0.001$, with CP control group: $p^{b} < 0.01$, n = 5 rats.P: significance level.

2.5.2. Tissue reduced glutathione (GSH) Concentrations

The results obtained indicate that the GSH concentration decreased highly significantly ($p<0.01$) to very highly significantly ($p<0.001$) in the heart and kidneys, and non-significantly ($p>0.05$) in the liver, respectively. The GSH concentration increased non-significantly ($p>0.05$) in the lungs of the CP group compared to the control group. However, treatment with CP+DF-ZnNPs increased the GSH content very highly significantly ($p<0.001$) in the heart and kidney, and non-significantly ($p>0.05$) in the liver, and decreased significantly ($p>0.05$) in the lungs compared to the CP group. As for the group CP+DF , there was a highly significant increase ($p<0.01$) in the concentration of GSH at the heart level and a non-significant increase ($p>0.05$) at the liver and kidney level. It also decreased at the lungs in a non-significant way ($p>0.05$) compared to the CP group.

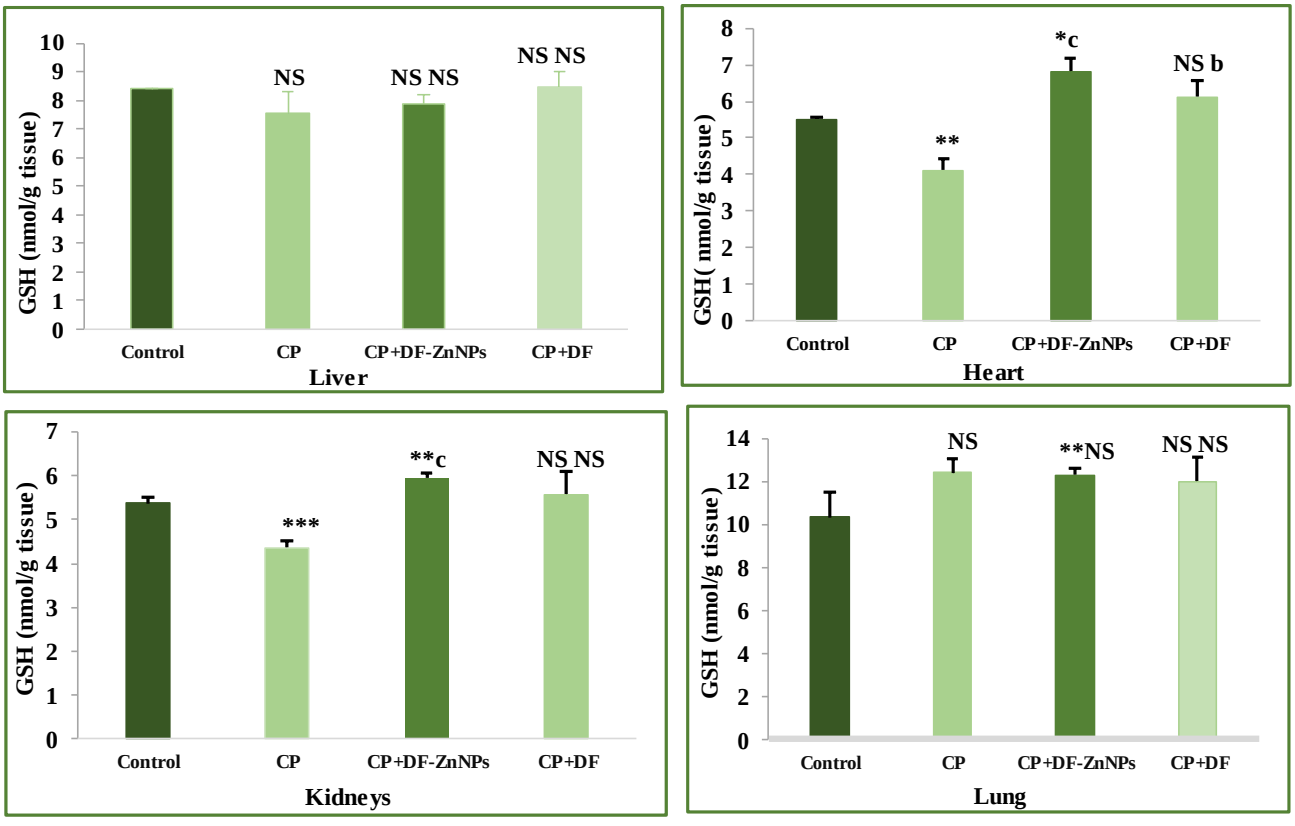

Figure 20: Tissue Reduced Glutathione (GSH) Concentrations in control and experimental groupsComparison with control group: * $p < 0.05$; $p^{**} < 0.01$, with CP control group: $p^{b} < 0.01$, $p^{c} < 0.001$, n = 5 rats.P: significance level.

2.5.3. Super oxide dismutase activity (SOD)

SOD activities in the heart and lungs showed ahighly significant increase ($p < 0.01$), and in the liver and kidneys they decreased in a very highly significantly way ($p < 0.001$) in the CP group compared to the control group. In addition, compared to the CP group, SOD activity increased in a highly significantly way ($p < 0.01$) in liver and non-significant increase ($p > 0.05$) in the kidneys, on the contrary decreased significantly ($p <0.05$) in the lungs and a highly significantly way ($p < 0.01$) in the heart for the CP+DF-ZnNPsgroup. As for the CP+DF group, SOD activity in the liver increased in a highly significantly way ($p <0.01$), and a very highly significantly way ($p < 0.001$) in the liver and kidneys respectively. On the contrary, there was a decrease but non significantly ($p > 0.05$) in the lungs. While no significant changes ($p > 0.05$)

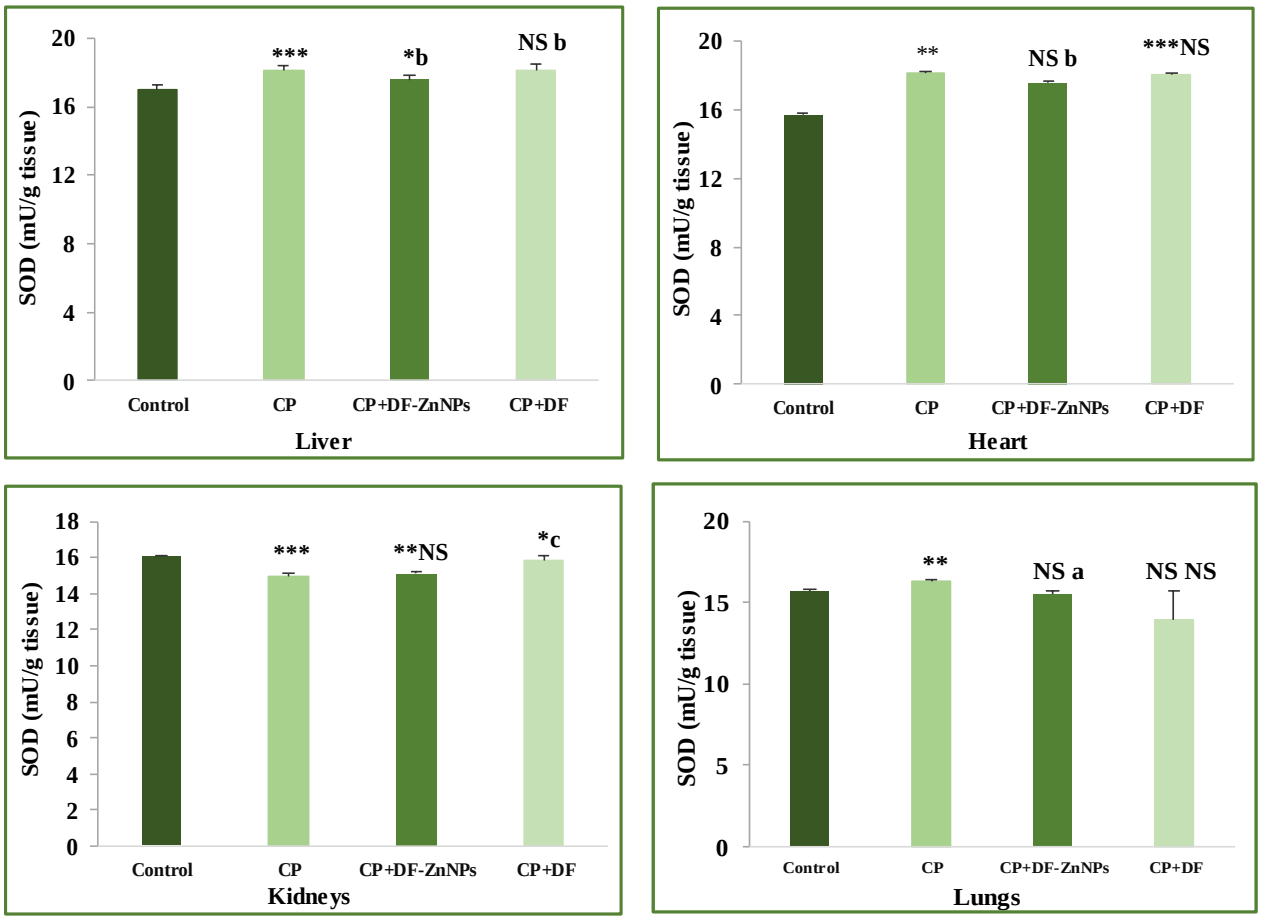

Figure 21: Tissues SOD activity in control and experimental groups.

Comparison with control group: * $p < 0.05$, $p^{**} < 0.01$, $p*** < 0.001$, with CP control group: $p^{a} < 0.05$; $p^{b} < 0.01$, $p^{c} < 0.001$, n = 5 rats.P: significance level.

3.Histopathological study

3.1.Histopathological examimination of the kidneys

Figure 22 present the histological analyzes from different groups of the kidneys of rats from different groups. Light microscopic examination of a kidney section from the control group reveals a very healthy structure, free of various abnormalities, with a normal renal cortex and glomerulus with a narrow Bowman's space, as well as convoluted proximal and distal tubules. On the other hand, cisplatin administration to rats revealed several adverse histological changes and lesions. The kidney section shows tubular necrosis with dilated Bowman's space and distorted glomeruli.

Furthermore, histological observations of the kidney sections of rats treated with CP+DF-ZnNPs demonstrate complete restoration and improvement of the kidney structure, with the glomerulus having a normal structure. The tubules have a relatively regular and distinct lumen. The lobular organization of the glomerulus can be seen, and there are no obvious signs of inflammation, necrosis, or hemorrhage, indicating healthy renal function.

Finally histological findings of CP+DF treated rats indicate partially improved morphology and restoration of glomerular structure, with infiltration of inflammatory cells surrounding the glomeruli and distorted tubules due to the effect of cisplatin.

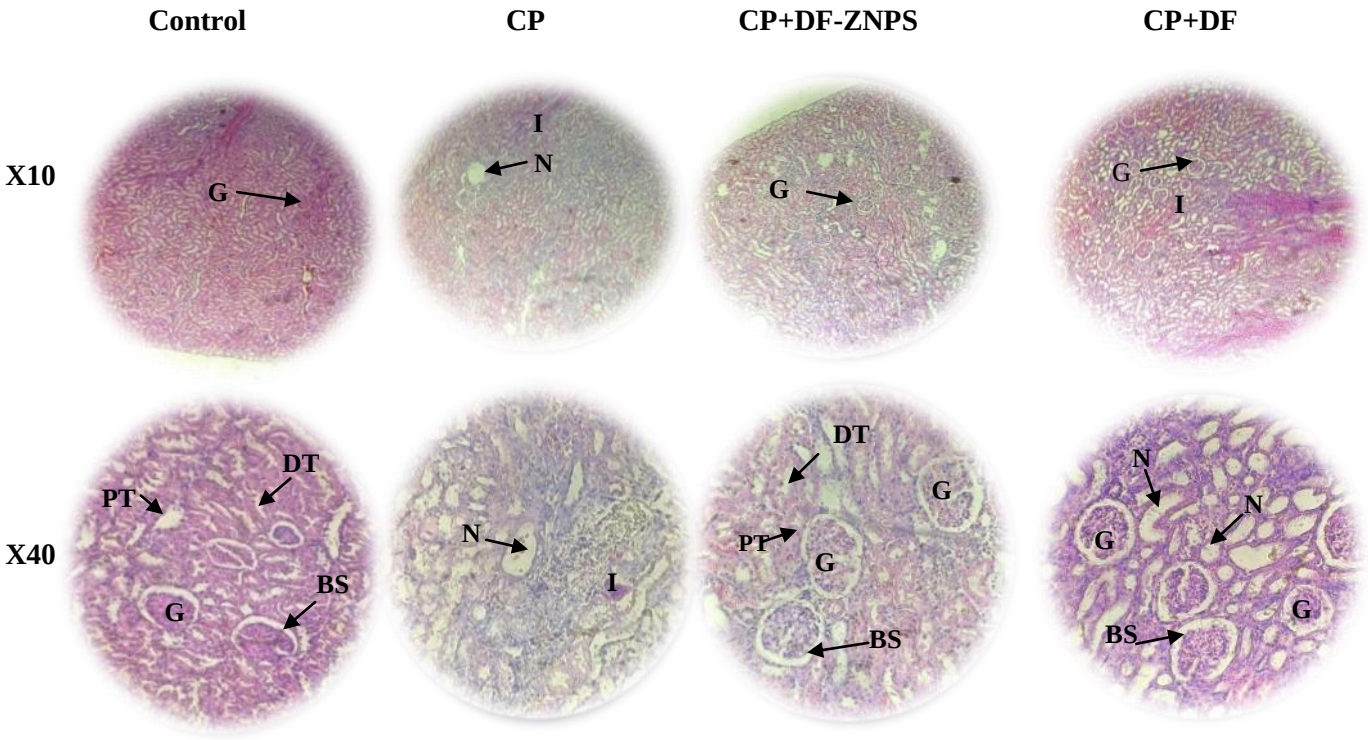

Figure 22: Representative photomicrographs of kidney sections of rats from the different experimental groups stained with hematoxylin and eosin stain

G: Glomerulus, **BS:** Bawman's space**, PT:** Proximal tubules**, DT:** Distal tubules **I:** Inflammation**, H:** Hemorrhage**, N:** Necrosis

3.2.Histopathological examimination of the liver

Figure 23 illustrates the histological analyzes of liver from different groups. The control group shows normal liver tissue. Hepatocytes appear healthy, with well-defined nuclei and cytoplasm. Sinusoids (the bloody spaces between hepatocytes) are clearly visible and appear normal.

With cisplatin administration, cellular damage is more pronounced. Some hepatocytes show signs of degeneration or necrosis, including sinusoidal dilation, altered cellular morphology, and inflammatory cell infiltration.

Furthermore, histological observations of liver sections from rats treated with CP+DF-ZnNPs show partially restored liver structure and reduced sinusoidal dilation.

As for the CP+DF group, there was a relative recovery in the structure, with necrosis in the liver tissue and clear erosion in the liver cells due to the effect of cisplatin.

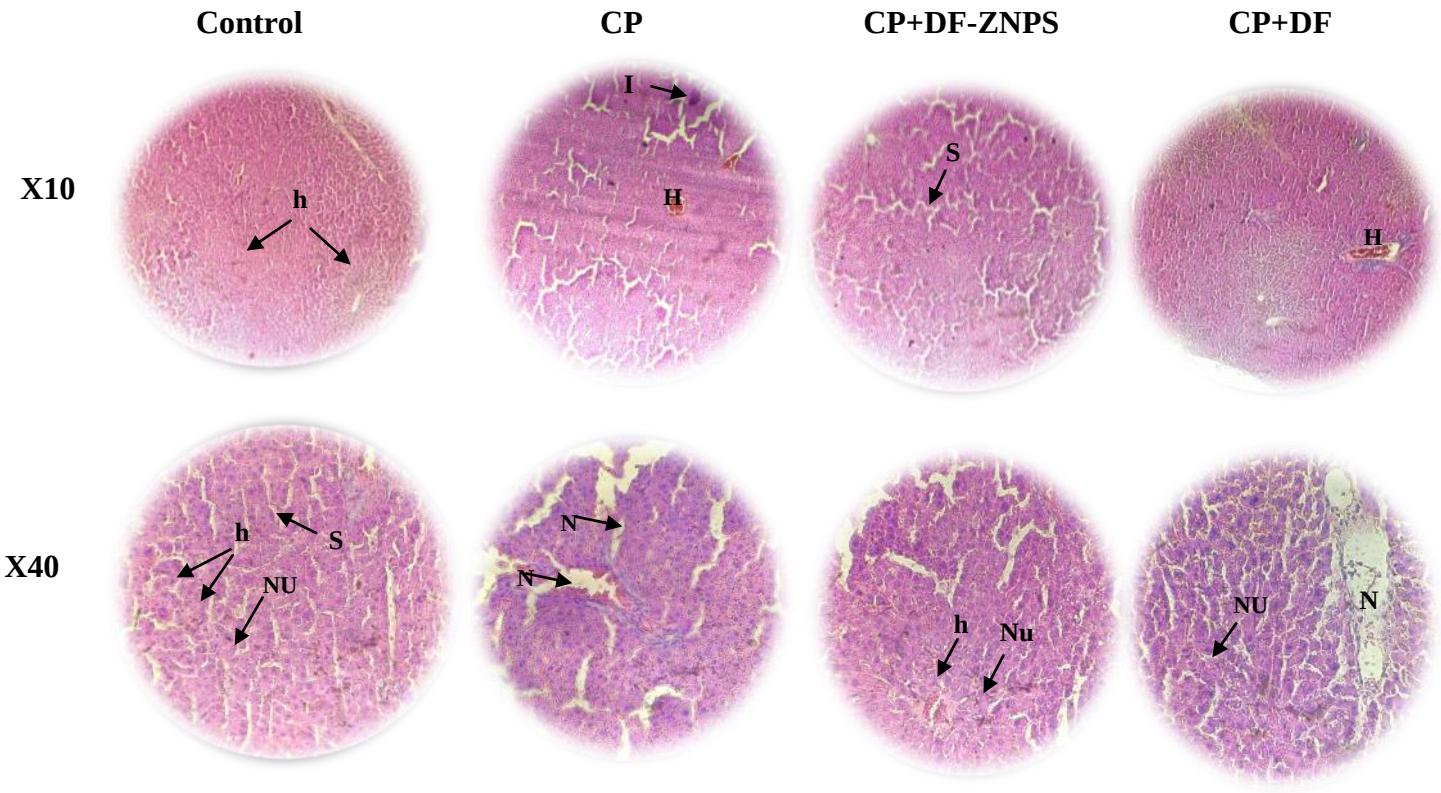

Figure 23: Representative photomicrographs of Liver sections of rats from the different experimental groups stained with hematoxylin and eosin stain

S: sinusoids**,h:** hepatocytes**, Nu:** Nucleus**.I:** Inflammation**, H:** Hemorrhage**, N:** Necrosis

3.3.Histopathological examimination of the lungs

Figure 24 Clarify the histological analyzes of Lung from different groups. The lung tissue in the control group appears to have a relatively regular structure of Bronchial. Thin-walled alveoli and clear air spaces can be observed. The blood vessels appear normal. On the other hand, the lung of cisplatin-treated rats showing severe hemorrhage, necrosis, inflammatory leukocytic infiltration, intense interstitial fibrosis, vascular fibrosis.

Furthermore, histological observations of the lung CP+DF-ZnNPs-treated rats showing decreasing hemorrhages and increased alveolar sacs, decreasing fibrosis, and the number

reducing of inflammatory cell infiltration. For the CP+DF group , Shows a relative decrease in peribronchiolar hemorrhage, erosion of the pulmonary tissue.

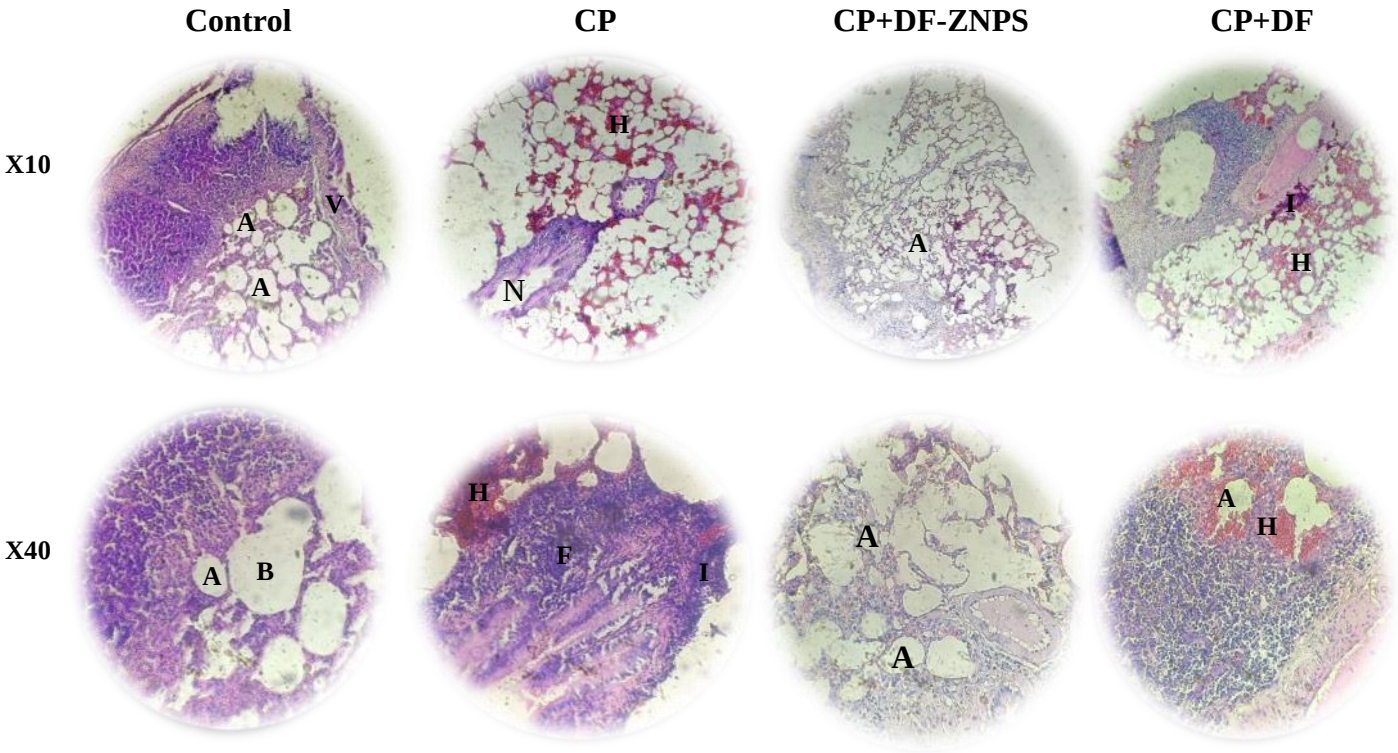

Figure 24 Representative photomicrographs of Lungs sections of rats from the different experimental groups stained with hematoxylin and eosin stain

A:Avioli, B:Bronchial,**V:**Vessel**, F:**intense interstitial fibrosis**, I:** Inflammation**, H:**Hemorrhage**, N:** Necrosis.

Chapter III

Discussion

Discussion

Cisplatin is a commonly used chemotherapeutic drug **(Romani, 2022)**. It is characterized by its alkylating property, directly interfering with DNA and inhibiting cancer cell division **(Sinitsyna et al., 2022)**. It is primarily active in the liver after exposure to water, where ions are exchanged within the compound, making it active and capable of interacting with the DNA of target cells **(Pietrangelo & Gatti, 2021)**. Cisplatin stimulates the production of reactive oxygen species (ROS) within cells, leading to oxidative stress. This stress causes tissue damage through the oxidation of biological molecules such as proteins, lipids, and DNA, promoting cytotoxicity and leading to cell death in various organs such as the kidneys, heart, and lungs. The damage resulting from oxidative stress contributes to the toxic side effects associated with cisplatin use, such as nephrotoxicity, cardiac dysfunction, and pulmonary toxicity, limiting its safe use **(Rehman & Shah, 2021)**. In this experiment, it was used to stimulate an immune response in rats. We used natural products containing ZnNPs along with natural camel hump fat to evaluate their therapeutic effect. Several in vitro and in vivo tests were conducted to confirm the effects of these products.

1. Characterization of nanoparticles

GC-MS analysis indicated that The chemical constituents of DF-ZnNPs were pentadcanoic acid methylester, Benzoic acid-methylester, Tetradecanoic Acid 12 methyl- methyl ester, stearic acid methyl ester, cic-10-heptadecanoic acid-methyl ester, 9,12-octadecodienoic (Z,Z) (linoleic acid methylester). The present study proved that DF-ZnNPs may Possesses good antifungal and antimicrobial activity. This may be due to the presence 9,12 –octadecodienoic acid (Z,Z) and pentadcanoic acid methylester against several bacteria such as E. coli and B. subtilis (Fatema et al.,2019).The DF-ZnNPs contains also Tetradecanoic acid which have antioxidant and antimicrobial properties **(Muzahid et al.,2022)**.

We employed FT-IR spectroscopy to verify that ZnNPs were prepared successfully. In line with the findings of Derouiche et al **(Chetehouna et al.,2020)**, there is a peak in the 400–700 cm-1 range.With the use of FT-IR analysis, several functional groups in ZnO NPs were discovered. Other peaks could be the result of C-O (ether group) or C-N (amine group) vibrations. Additionally, the area beneath 1000 cm-1 exhibits a number of peaks. Zinc oxide (Zn-O)

vibrations and the molecule's "fingerprint" are the causes of these peaks. The Zn-O stretching vibration was identified as the cause of the peak at 500 cm^{-1}. TEM and SEM examination were used to examine the morphology and average particle size. The results indicated that ZnO NPs were spherical in shape and had an average size of 2.67 ± 0.96 nm, but the sizes of the zinc nanoparticle modified with fatty acids ranged from 26.7 to 41.7 nm **(Matei et al.,2024)**. An analytical technique called energy-dispersive X-ray spectroscopy (EDS) makes it possible to determine a sample's elemental composition **(Dasgupta & Wahed,2021)**. The successful production of zinc oxide (ZnO) nanoparticles was verified by the application of energy-dispersive X-ray spectroscopy (EDS). The ZnO nanoparticles were found to contain 27.1% oxygen and 72.9% zinc, according to the elemental analysis. Zinc had the strongest intensity peaks at energy levels of 0.92 keV, 8.83 keV, and 9.61 keV, whereas oxygen showed the strongest intensity peak at 0.5 keV. Zinc's maximum intensity peaks were observed at 1 keV, 8.7 keV, and 9.8 keV, respectively, in a different investigation **(Alharbi et al.,2023)**.

2. Antibacterial activity

Zinc nanoparticles biosynthesized using camel fat exhibited superior antimicrobial activity against multidrug-resistant bacteria compared to their chemically synthesized counterparts, indicating their retention of the bioactive components of the lipid matrix **(Mohammed & Al-Qahtani, 2023)**. Nanoparticles (NPs) are increasingly used to target bacteria as an alternative to antibiotics. Nanotechnology may be particularly advantageous in treating bacterial infections. Examples include the utilization of NPs in antibacterial coatings for implantable devices and medicinal materials to prevent infection and promote wound healing, in antibiotic delivery systems to treat disease, in bacterial detection systems to generate microbial diagnostics, and in antibacterial vaccines to control bacterial infections **(Nasrollahzadeh et al.,2019)**.Earlier in 2009, Liu et al. checked the antibacterial activities of ZnONPs (70 nm & spherical) against *Escherichia coli* (gram negative). ZnONPs showed a dose-dependent growth inhibition of *Escherichia coli* treated with 3-12 mM concentration for 24 hrs, and a complete growth inhibition was observed at 12 mM concentration **(Liu et al.,2009)**. ZnONPs caused destruction of proteins and lipids on bacterial cell membrane, leading to a damage of the bacterial cell membranes with leakage of intracellular contents and death **(Al-Harbi et al.,2022)**. In 2010, Sevinç and Hanley. Checked the antibacterial effect of resin-based dental composites blended

with ZnONPs (40 -100 nm & Elongated shape) **(Aydin Sevinç & Hanley 2010)**. They observed that the composites with increasing amount of ZnONPs (1, 5 and 10 %) inhibited S. sobrinus (gram positive) biofilm formation for 3 days in a dose-dependant manner as compared with unmodified composites **(Kumar &Yadav,2014)**. Li et al, demonstrated the bacterial growth inhibition effect of ZnONPs (100 nm & irregular shape) coated poly (vinyl chloride) films against both *E. coli* or *S. aureus*, and the antibacterial activity was further improved by 26.0% and 29.8% for S. aureus and *E. coli*, respectively when exposed with UV light **(Verma et al.,2017)**.

3. Biochemical and enzymatic parameters

Despite the strong effect of cisplatin, it has side effects of liver and kidney toxicity **(Arany & Safirstein,2003)**. These facts are consistent with the results of our study,where we observed a significant increase in transaminases activities. Various studies have demonstrated evidence of cisplatin-induced liver injury **(Liao et al.,2008)**. Martinez et al. reported that cisplatin-induced hepatotoxicity included membrane stiffening, lipid peroxidation, and oxidative damage to cardiolipin and protein sulfhydryl **(Martins et al.,2008)**. Işeri et al. found that a single intravenous injection of cisplatin at a dose of 2.5 (mg/kg) body weight in Sprague-Dawley rats impaired liver function and caused significant increases in serum ALAT and ASAT levels **(Işeri et al., 2007)**.In a study, it was found that CP causes liver toxicity, leading to increased levels of the enzyme biomarkers ASAT and ALAT, which are associated with the degree of liver damage **(Palipoch & Punsawad,2013)**.In this study, CP causes a induced hepatotoxicity manifested by increased serum ALAT and ASAT levels **(Abouzeinab,2013)** Our results confirm the previous reports of **(Mansour et al.,2006)**, and **(Lee et al.,2007)**, who reported of CP to significant impairment of liver function, as assessed by increased ALAT and ASAT levels. Therefore, it can be suggested that hepatocytes are more susceptible to CP toxicity. Consequently, the ability of CP to induce a marked increase in ASAT and ALAT enzyme activity may be a secondary event following CP induced liver damage, with subsequent leakage of ALAT and ASAT from altered hepatocytes. The alteration in the liver function parameters induced by cisplatin is closely associated with an increase in reactive oxygen species (ROS) and lipid peroxidation in the liver tissue **(Silici et al.,2011)** The increased activity of ALAT, and ASAT has been attributed to the destroyed structural integrity of the liver, because these are normally located in the cytoplasm and

are released into the circulation after hepatic damage **(Garba et al.,2009)**. These findings may refer to degenerative changes and hypo function of the liver **(Abdel-wahhab & Aly,2009)** and also hepatic cell necrosis which increases the release of these enzymes in the blood stream **(Singh et al.,2005)**. The increasing levels of these enzymes in the serum are presumptive signs of cisplatin induced necrotic lesions in the hepatocytes **(Jaramillo- Juárez et al.,2008)**. As for our results, the Df-ZnNPs treatment were able to reduce ALAT and ASAT levels by varying degrees and with a clear difference. As zinc treatment corrects plasma enzyme activities, which may be attributed to the free radical/antioxidant and chelating properties of this element **(coni et al., 2021)** and cell membrane stability. Thus, zinc has a hepatoprotective effect in various toxic conditions. These results are consistent with previous research indicating that zinc has a positive effect on histological and enzymatic changes in rats **(Kataba et al., 2021**).

CP causes an increase in creatinine levels **(Volarevic et al., 2019)**. These findings are consistent with the results of this study, in which we observed a significant increase in creatinine levels in the CP group compared to the control group. Elevated serum creatinine is an indicator of renal dysfunction **(Ozkok & Edelstein, 2014)** The kidneys are affected by cisplatin through tubular necrosis, detachment of tubular cells from the basement membrane, and the presence of protein casts in the tubular lumen **(Mohamadi Yarijani et al., 2018)** This drug affects the proximal and distal convoluted tubules of the kidney by inducing apoptosis, DNA damage, and oxidative stress, which increases reactive oxygen species and inflammation **(Liu et al., 2012)** These results indicate that cisplatin is responsible for raising creatinine levels and causing renal dysfunction **(Sultana et al.,2022)** .

On the blood sugar levels, the CP group showed a clear difference in the results compared to the control group, this is because cisplatin is able to increase inducible nitric oxide synthase and somatostatin in pancreatic islets **(Wang & Aggarwal ,1997)**. Somatostatin and nitric oxide inhibit insulin secretion **(Nilsson et al.,1989)**, and nitric oxide is considered a major causative factor of insulin-dependent diabetes **(Corbett et al.,1993)**. However, the Df-ZnNPs system reduced blood sugar, that is because ZnNPs lead to an increase in glucose absorption in the liver and its storage **(Hussein et al.,2014)**.

On the levels of cholesterol (TC) and triglycerides (TG), CP group showed differences in the results compared to the control group. This indicates the presence of liver disorders **(Atawodi et al.,2014)**. The increase in serum TC and TG levels after exposure to CP can be attributed to its harmful effect, which leads to liver dysfunction and impaired lipid metabolism, which is consistent with the results of **(Akindele et al.,2014)**, as the liver produces TG and incorporates it into very low-density lipoprotein cholesterol (VLDL) for transport to peripheral tissues **(Parinita ,2012)**. When liver injury occurs, its ability to produce it is impaired, leading to an increase in TG **(Manninen et al.,2002) .** In contrast, Df-ZnNPs reduced the levels of both TC and TG. Zinc plays a role in enzymatic actions, as it is an integral part of many of them that participate in fat digestion and absorption **(Abd El-Hack et al.,2017**).

4. Hematological parameters

Chemotherapeutic medications are usually cytotoxic, meaning they kill cancer cells while, also destroying the immune system. Bone marrow cells, depending on their proliferative nature, are extremely sensitive to cytotoxic substances and vulnerable to DNA damage, especially undifferentiated populations **(Shaymaa et al., 2017**). Cisplatin is one of alkylating agents that directly damage DNA resulting in cell apoptosis. Like most of chemotherapeutic drugs; cisplatin does not distinguish between cancer and normal cells and eliminates not only the fast-growing cancer cells but also other fast-growing cells in the body **(Salam et al., 2012**).

Cisplatin causes the generation of reactive oxygen species (ROS) and to inhibit the activity of antioxidant enzymes in the blood *tissue* **(Ghosh et al.,2005*)*,** It is reported that ROS increase hemoglobin glycation and erythrocyte fragility **(Niforou et al.,2014*)*** More specifically hemoglobin-derived iron might contribute to the pathogenesis of cisplatin by inducing oxidative stress **(Baliga et al.,1998)**.Thus, cisplatin-induced Hb reduction is related to suppression of erythropoiesis and iron supply to erythroblasts **(Cazzola,2000)**. The fall of Hct is a reason for the decreased erythrocyte number **(Harris et al.,2002**).

Inhibition of cell proliferation is one of the major causes of cisplatin induced myelotoxicity **(Basu et al., 2015)**. The reduction in these values in the present study might be due the effect of cisplatin on bone marrow. There was an etiological relationship between anemia and CP treatment. Such relationship could be explained through different mechanisms including

destruction of bone marrow cells or increase osmotic fragility of RBCs. Thus, CP intoxication might lead to anemia as a result of either suppression the activity of hematopoietic tissues, impaired erythropoiesis, and accelerated RBCs destruction because of the altered RBCs membrane permeability (Hassan et al., 2010). According to **(Nowis et al.,2007)**, cisplatin injection decreased erythropoietin, a haemopoietic growth factor, causing haematological parameters to change. CP generates oxidative stress platelets and lymphocytes, according to **(Olas et al.,2005)**, which could affect their function.which of course leads to lower levels of red blood cells,hemoglobin and hematocrit.which explains our results. All immune cells and red blood cells of the CP group showed a clear difference compared to the control group.This is consistent with a (2014) study in which a dose of 7.5 mg/kg cisplatin there was a Reduction in RBCs, at both the 8^{th}And 13^{th} days of the trial, the Cisplatin-treated group exhibited a Substantial detrimental effect on Haematological parameters **(Nasr, 2014**). During an experience for **(Rajendrakumar et al., 2020)**. CP caused A substantial decrease in Hb, RBCs and total platelet. **(Ramya et al.2013)** showed similar Changes in blood parameters after Cisplatin treatment. **(Karale & Kamath ,2017)** and **(Lin et al.,2018)**.

In contrast to platelet and white blood cell levels,which are supposed to decrease,As in a study by **(Adaramoye et al.,2008)** mentioned That the apoptotic impact of Cisplatin on lymphocytes and Platelets resulted in lymphopenia And thrombocytopenia in the Cisplatin-treated group, resulting in A reduction in the amount of these Cells in the blood. The CP group showed higher white blood cell and platelet counts compared to the control group. We can explain this significant increase in the CP group as a result of infection and inflammation **(Markovic et al., 2011)**. And CP metabolism **(Olas et al.,2005)**. On the other hand, one researcher reported that the platelet count in cisplatin group was also higher than that in the control group **(Masamatti &Vijaya,2018)**.This may be due to reactive thrombocytosis resulting from the resulting anemia. The negative effect on erythropoietin production resulting from anemia may be responsible for the thrombocytosis **(Hoffbrand et al.,2001)**.

RBC are the most abundant cells in the body. They contain the protein hemoglobin, which is mainly responsible for transporting O2 from the lungs to the rest of the body. It also fixes CO2 to expel it from the body **(Ismail et al.,2023**). Which means that low levels of RBC can lead to disaster in the body: hypoxia, cardiovascular disease **(Kuhn et al.,2017)**. This applies to the CP

group, which showed low levels of erythrocytes and hemoglobin. We previously explained that low levels of RBC in this group results from the apoptosis of haematopoietic cells. In our study, Df-ZnNPs were able to restore red blood cell values to normal levels, which we explain by reaching an appropriate amount of zinc for red blood cells, as zinc enables the bone marrow to form new red blood cells even after exposure to anemia **(Chen et al., 2020**).

5. Oxidative stress parameters

Cisplatin is one of the most widely used and effective chemotherapeutic drugs, used to treat a range of tumors, including testicular, ovarian, lung, and bladder cancers **(Alassaf & Attia, 2023)**.CP works by binding to the DNA of cancer cells, preventing their division and ultimately leading to apoptosis **(Arany& Safirstein, 2003)**.Despite its effectiveness, its use is associated with serious side effects, most notably liver and kidney toxicity **(dos Santos et al., 2012)**.Evidence suggests that oxidative stress is a major mechanism behind these toxicities **(Chirino & Pedraza-Chaverri, 2009)**.Cisplatin stimulates the production of reactive oxygen species (ROS), such as hydrogen peroxide and hydroxyl radicals, which damage DNA, proteins, and lipids **(Pabla & Dong, 2008)**. It also reduces intracellular levels of antioxidants such as glutathione (GSH) and inhibits enzymes such as superoxide dismutase and catalase, disrupting the balance between oxidants and antioxidants **(Zhang et al., 2023).** As a result, research has begun to focus on the use of natural antioxidants as protective agents, which have shown efficacy in reducing this toxicity **(Alanezi et al., 2022**).

Zinc nanoparticles have shown improved performance, immunity, and antioxidant capacity **(Aioub et al., 2022)**.

In this study, oxidative stress of liver, kidney, heart, and lung tissues was evaluated by determining the values of: MDA a product of lipid peroxidation **(Całyniuk et al.,2016**), SOD an antioxidant enzyme involved in combating oxidants in the body (**Ighodaro &Akinloye,2018)**, and GSH involved in protection against oxidative damage **(Bhagat et al., 2016)**.

In this study, we observed elevated malondialdehyde levels in all organs of mice injected with CP. Malondialdehyde (MDA) is a biomarker of oxidative stress **(Wang et al., 2021)** and also increases pro-inflammatory cytokines **(Mueangson et al., 2023)**. This phenomenon may be

attributed to the potential consumption of antioxidants to alleviate CP-induced oxidative stress. The increased production of reactive oxygen species (ROS) during injury threatens reactive molecules by damaging nucleic acids, oxidizing proteins, and causing lipid peroxidation, thus raising MDA levels **(Bahrami et al., 2016)**. These results are consistent with the study by **(Ürün et al., 2024**). According to several researchers, there is a connection between MDA and difficulties brought on by cisplatin **(Antunes et al., 2000; Silva et al.,2001)** Reduced antioxidant synthesis in tissues that have been exposed to Cisplatin as a result of increased ROS activity. one explanation for the increase in MDA Concentration **(Chen et al.,2007)**.

Our results showed a significant decrease in GSH levels in all affected organs except the lung. This is consistent with the results of a study by **(Huang et al., 2024**). Glutathione (GSH) is the most abundant low-molecular-weight thiol, and its deficiency can cause oxidative stress (Wu et al., 2004). Cisplatin binds to sulfhydryl groups **(Dedon & Borch, 1987)**. Cisplatin-induced nephrotoxicity and renal cell death were found to be associated with decreased mitochondrial glutathione (GSH) and NADPH levels, decreased glutathione to GSSG ratio, loss of mitochondrial membrane potential, cardiolipin oxidation, and caspase-3 activation, with glutathione depletion and increased GSSG levels, due to decreased cisplatin-induced glutathione reductase activity **(Santos et al., 2007)**.

Superoxide dismutase (SOD) acts as a crucial defense mechanism against oxidative stress by scavenging potentially harmful free radicals **(Abdulgafor et al., 2018)**. According to **(Almaghrabi, 2015),** superoxide radicals, either alone or in combination with H2O2, induce the oxidation of catalase (CAT) and glutathione peroxidase (GSH-Px), which subsequently leads to a decrease in SOD activity. This finding is consistent with our observations, as we recorded decreased SOD activity in two organs, the liver and kidney, of the CP group. These results are consistent with those of **(Kaya et al., 2024**). Furthermore, decreased SOD activity is associated with increased inflammatory processes **(Huang et al., 2017**).

Our results show a decrease in MDA levels in the liver, heart, and lung of the Df-ZnNP group compared to the CP group. These results indicate a decrease in oxidative stress. There was also an increase in GSH levels in the heart and kidneys. GSH plays a role similar to catalase in converting H2O2 to H2O and provides another detoxification pathway **(Rajashekaraiah et al., 2021**). In addition, our data recorded a significant increase in SOD levels in the liver, heart, and lung of the Df-ZnNP group.This decrease caused by Df-ZnNPs can be attributed to the unique composition and properties of camel hump fat **(Jassim et al., 2018**). In addition **(Bąkowski et al., 2018)** explained that Zn is a strong antioxidant metal decreasing free radicals. It has also been reported that nano-ZnO can increase antioxidant activity and decrease free radicals due to the increased specific surface area and thus the higher number of active sites.

6. Histopatological analysis

After inducing an immune response by CP injection, Bowman's space dilation and glomerular distortion with necrosis and inflammation were observed in the kidneys. Furthermore, hepatocyte degeneration occurred with inflammation, necrosis, and hemorrhage. Similar findings were reported in **(Bakır et al., 2015)**. CP-induced liver toxicity included membrane sclerosis, lipid peroxidation, and oxidative damage to cardiolipin and protein sulfhydryl groups **(Martins et al.,2008)**. Previous data showed increased levels of MDA, a biomarker of lipid peroxidation, and decreased levels of GSH, catalase, and SOD in liver and kidney tissues, indicating toxicity resulting from oxidative stress **(El-Beshbishy et al., 2011; Kim et al., 2004)**. Furthermore, increased spatial markers, including ASAT and ALAT, correlated with the degree of liver damage **(Liao et al.,2008)**. The underlying mechanism is CP-induced oxidative stress. Through the increase in reactive oxygen species (ROS) levels and the decrease in the antioxidant defense system **(Chirino et al.,2009)**. **(Jiang et al.,2007)** also showed the potential role of ROS species in the activation of p53 protein and cell. The results showed the presence of inflammation, necrosis and hemorrhage in the lung tissue. Our results were consistent with a study by **(Geyikoglu et al., 2017)**.

The lungs are cilia-rich organs, and ciliated cells are predominantly found in the airway epithelium **(Bustamante-Marin & Ostrowski,2017)** Ciliary movement protects the lungs from various pollutants, including oxidizing agents, by releasing inhaled harmful molecules **(Price & Sisson ,2019)**.Tilley et al. reported that a variety of external factors, including contaminants,

microbes, or lifestyle factors, cause dysfunctions of the cilia, which is associated with various lung diseases **(Han et al.,2021)** Recently, Price et al. reported that ciliopathy is caused by impairment of the redox balance **(Han et al.,2017)**. Furthermore, the activity of dynein, a molecular motor and a regulator of ciliogenesis, is reportedly affected by changes in redox status **(Kim et al.,2013)**. Cisplatin weakens oxidation and reduction in the lung and increases the number of reactive oxygen species, which leads to oxidative stress and consequently damage to lung cells and disruption of cilia **(Kong et al.,2019)**.

Histological sections of rats treated with Df-ZnNPs showed a significant improvement. This may be explained by the anti-inflammatory and antioxidant effects of polyunsaturated fatty acids (PUFAs) through inhibiting lipid peroxidation. Their protective effects against liver fibrosis have also been demonstrated. Furthermore, PUFAs improve antioxidant status by activating the NRF2 (nuclear factor erythroid factor 2-related factor) pathway, which can regulate the detoxification of reactive oxygen species (ROS) **(Xu et al., 2023).** In addition,the effect of zinc, which is an essential component of many metalloenzymes and nuclear enzymes **(Hussain et al.,2022)** and helps in the development of the immune system through cell production, DNA replication, and cell division (**Šimić et al.,2019)**. Therefore, as a structural component of the antioxidant enzyme SOD, it ameliorates oxidative damage from ROS. The presence of SOD in the cell is responsible for converting superoxide radicals into H2O2 and molecular oxygen. This is a potential mechanism for ameliorating ROS and protecting the cell **(Cruz et al.,2015**). Therefore, Df-ZnNPs may mitigate cisplatin-induced oxidative damage and improve tissue quality.

Conclusion

Conclusion

Chemotherapy is a primary method of cancer treatment. However, despite its effectiveness in combating tumors, it causes numerous harmful side effects, particularly on the immune system. This makes the search for innovative solutions to improve these effects an urgent necessity. In this context, nanotechnology emerges as a promising solution that offers unlimited possibilities for improving the effectiveness of chemotherapy treatments. Nanoparticles are characterized by their ability to precisely interact with cells and tissues, allowing them to direct treatment more precisely and effectively to the targeted areas, thereby reducing side effects and increasing the therapeutic effect.

- The successful biosynthesis of zinc nanoparticles (DF-ZnNPs) using dromedary camel hump fat was confirmed in our study using UV-Vis spectroscopy, FTIR spectroscopy, scanning electron microscopy (SEM/EDX), transmission electron microscopy (TEM), and gas chromatography-mass spectrometry (GC-MS). DF-ZnNPs also exhibited antibacterial activity. These results highlight the potential of zinc nanoparticles as an alternative to conventional antibacterial drugs in combating antibiotic-resistant organisms.

- In vitro studies on DF-ZnNPs demonstrated antibacterial activity against the studied bacterial strains. These results highlight the potential of DF-ZnNPs as an alternative to conventional antibacterial drugs in combating antibiotic-resistant organisms.

- Hematological analysis revealed a significant change among DF-ZnNPs-treated rats, demonstrating its effects on modifying anemia marker levels and modulating immune responses, leading to reduced inflammation.

- According to biochemical analysis, the damage caused by CP administration was reversed in the DF-ZnNPs-treated group, indicating that this treatment can adequately repair and protect organ damage.

- Current evidence concludes that DF-ZnNPs enhanced the activity of antioxidant enzymes, which may have protected Wistar rats from CP-induced oxidative stress.

- The effect of the studied treatments also extended to the microscopic level, resulting in partial healing of the studied tissues.

Finally, based on the above, the results indicate that DF-ZnNPs improved immune balance and enhanced the body's ability to cope with the negative effects of chemotherapy. Interestingly, they are made from natural materials, which reduces their side effects and facilitates their use.

Perspectives:

This study can be expanded to include the synthesis of other metallic nanoparticles, such as silver or copper, using camel fat or other lipid-rich natural fatty materials.

-Conduct seversl other tests for DF-ZnNPs for example test anticancer.

- Potential industrial valorization of camel hump fat as a bio-based nanomaterial source, supporting green nanotechnology and sustainable innovation in regions where camels are economically and culturally significant.

- Rigorous clinical testing and evaluation to assess the effectiveness, safety, and optimal administration of DF-ZnNPs.

- These future studies will encourage further research into the valorization of traditional biological resources in nanotechnology, and the reduction of chemicals that are harmful to the body.

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