Republic of Iraq

Ministry of Higher Education

And Scientific Research

University Of Anbar

College of Science

Department of Chemistry

Synthesis and Characterization of Platinum Nanoparticles using Iraqi Dates Extract and Study of its Medical Applications

A Thesis submitted to

The Council of the College of Science -University of Anbar as a Partial Fulfillment of the Requirements for the Degree of Master in chemistry

By

Nasreen Hassan Ali Al-Jumaily

B.Sc. in chemistry 2002

Supervised by

Prof. Dr. Ahmed Mishaal Mohammed

University of Anbar-College of Science

2021 A.D **1442 A.H**

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

﴿وَيَسْأَلُونَكَ عَنِ الرُّوحِ

قُلِ

الرُّوحُ مِنْ

أَمْرِ

﴿وَمَا أُوتِيتُمْ مِنَ الْعِلْمِ إِلَّا قَلِيلًا﴾

صدق اللَّهُ العظيم

الإسراء: 85

Nasreen Hassan Ali

Department of Chemistry – College of Science

Synthesis and characterization of Platinum nanoparticles using Iraqi dates extract and study of its medical application

Supervisor Certification

I certify that this thesis was prepared under my supervision at the Department of Chemistry - College of Science - University of Anbar by **Nasreen Hassan Ali** in partial fulfillment of the requirements for the Degree of Master of Science in Chemistry.

Signature:

Name: **Dr. Ahmed Mishaal Mohammed**

Date: / / 2021

Head of Department Certification

Given the available recommendations, I forward this thesis for debate by the examination committee.

Signature:

Name: **Dr. Ahmed Mishaal Mohammed**

Date: / / 2021

Examining committee certificate

We, the members of the examining committee, certify that after reading this thesis entitled **"Synthesis and characterization of Platinum nanoparticles using Iraqi dates extract and study of its medical applications"** and have examined the student **(Nasreen Hassan Ali)** in its contents, that in our opinion, it is accepted as a thesis for the degree of master of science in chemistry.

Signature:
Name: **Dr. Dia Hadi Hussein**
(Chairman)
Title: **Professor**
Address: College of Science/
University of Mustansiriya
Date: / / 2021

Signature:
Name: **Dr. Juman Ahmed Nasser**
(Member)
Title: **Assistant Professor**
Address: College of Education for
Pure Science/ University of Baghdad
Date: / / 2021

Signature:
Name: **Dr. Khaled Farouk Abdel Ghafour**
(Member)
Title: **Assistant Professor**
Address: College of Science/
University of Anbar
Date: / / 2021

Signature:
Name: **Dr. Ahmed Mishaal Mohammed**
(Member & Supervisor)
Title: **Professor**
Address: College of Science/
University of Anbar
Date: / / 2021

Approved of Dean
Signature:
Name: **Prof. Dr. Emad A. Mohammed Salih**
(Dean of the College of Science)
Date: / / 2021

Dedication

This thesis is dedicated to Almighty Allah for giving me the opportunity and making everything possible in my path. It is also dedicated to my dear family for their care and support and to my supervisor Professor Dr. Ahmed Mishaal Mohammed without whom this thesis would not see the light of the day.

Acknowledgment

First I want to express my best thanks to merciful Allah who have been giving me enough strength and patience to perform and accomplish my scientific project successfully. I wish to express my sincere gratitude and appreciation to my supervisor (Professor Dr. Ahmed Mishaal Mohammed), who suggested this project, gave the advice and the directions to accomplish my work. I thank him for being with me despite all the difficulties and the challenges that I faced during the two years that I studied. I thank him for his kind heart and the right choices that he made as Head of Department, I consider him my role model, all the love and respect to him from me.

I would like to thank Assistant Professor Dr. Khaled Farouk Abdel Ghafour, Rapporteur of the Department for Postgraduate Studies, for all his support and assistance.

I would like to thank the Council of Science college, University of Anbar for their cooperation with us. I would also like to thank the staff of the Chemistry Department for their advice, encouragement and support.

I cannot forget the favor and support of my husband, Dr. Firas Abdel Hamid. He has all my thanks and gratitude for his continuous support at this important stage of my life. I also like to dedicate my work to my children. I would like to show my love and appreciation to my beautiful family for their support, care and patience during this crucial stage of my life.

Finally, I would like to thank all my friends who were great companions through hard times, supported, encouraged, and helped me get through this agonizing period in the most positive way.

Abstract

Green nanotechnology is a technology that has revolutionized the field of manufacturing nanomaterials with distinctive characteristics, sizes and shapes whose efficiency is parallel or better than the materials prepared by traditional methods and because of the importance of nanomaterials in many fields, including the medical field. This method has been used to produce compounds that have safe therapeutic properties and have few side effects, in addition to high effectiveness.

The production of metal nanoparticles (MNPs) that have antibacterial activity is an additional approach to combating infections caused by antibiotic-resistant bacteria.

Platinum nanoparticles were prepared using green method using (Phoenix dactylifera L., var. Zahidi) and (phoenix dactylifera L., var. Khastawi) dates extract. platinum salts were successfully reduced to their corresponding PtNPs in the presence of aqueous dates extract which considers a rich source of phytochemicals that led to the reduction of Pt^{+4} to Pt^{0} atoms by providing electrons for these ions.

Green method is considered safe, rapid, and cost-effective in comparison to chemical and physical methods . Platinum nanoparticles used as bioactive cytotoxic nano-agents against Ovarian cancer and Oesophagel cancer . Also, the efficiency of PtNPs in inhibiting the growth of bacteria *Pseudomonas aeruginosa* and *Streptococcus pyogenes* .

To as-certain the formation of PtNPs, the UV-Visible spectra showed surface plasmon resonance (SPR) bands around 283 nm for PtNPs. The infrared absorption spectrum showed various peaks ranging from (400 - 4000) cm^{-1} that used to identify the functional groups responsible for reducing and capping of PtNPs. Transmission electron microscope (TEM) analysis showed that the PtNPs were spherical in shape. Atomic force microscope (AFM) screening shows the formation of nanoparticles with a diameter ranging from (30 - 40) nm .

The images of the scanning electron microscope (SEM) display nanoparticles within the effective range of nanomaterials (1-100) nm. X-ray diffraction examination also showed the formation of platinum nanoparticles by spectrum comparative to the standard confirmed spectrum of platinum particles produced in the experiments were in the shape of nanocrystals.

Cancer cells including the Ovarian cancer SKO-3 cell line and Oesophageal cancer SK-GT-4 cell line were exposed to a series of prepared platinum nanoparticle concentrations (0.00125, 0.0025, 0.005, 0.01) M, and the inhibition rate of growth in cells was measured for 72 hours. The cytotoxicity screening showed that there was a highly toxic effect on the cancer cells.

Pseudomonas aeruginosa and *Streptococcus pyogenes* were exposed to a series of concentrations from prepared platinum nanoparticles (0.00125, 0.0025, 0.005, 0.01) M. The results exhibited significant inhibitory activity and the rate of bacterial growth inhibition increased with increasing concentration.

It can conclude from this study that the preparation of PtNPs gives good and encouraging preliminary results for future work as an anti-cancer and anti-microbial agent.

List of Contents

List of Figures

List of Tables

List of Symbols and Abbreviation

Symbols and Abbreviation	Full name
AFM	Atomic force microscope
COVID-19	Coronavirus disease 2019
D	Dimension
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
EDTA	Ethylene diamine tetraacetic acid
FT-IR	Fourier transform infrared
GAS	group A beta-hemolytic streptococcus
GORD	gastro-Oesophageal reflux disease
MTT	Thiazolyl blue tetrazolium bromide
NMs	Nanomaterials
NPs	Nanoparticles
PtNPs	Platinum nanoparticles
PTT	photothermal therapy
P. aeruginosa	*Pseudomonas aeruginosa*
ROS	reactive oxygen species
RPMI	Roswell park memorial institute
RT	radiotherapy
S. pyogenes	*Streptococcus pyogenes*
SEM	Scanning electron microscope
SPR	surface plasmon resonance
16S rRNA	RNA component of the 30S small subunit of a prokaryotic ribosome
TEM	Transmission electron microscope
UV	Ultraviolet
XRD	X-ray diffraction
λ	the wavelength of the x-ray
d	the spacing of the crystal layers
θ	Theta

CHAPTER ONE

1. Introduction

1.1 Date palm

Date palm scientific name is *Phoenix dactylifera L*. Plantations exist in a number of regions of the globe. The date palm is one of the most famous trees in the Arab world in general, and in Iraq in particular, where it is considered the world's national tree [(1)].

The date palm is one of the Arab region's ancient fruit trees and is widely grown owing to its edible sweet fruit [(2)]. Date palm is a fruit tree that is resistant to unfavorable climatic conditions in the hot desert areas of the Middle East and North Africa [(3)].

In the majority of Arab countries, date palm is a major fruit crop. Iraq is one of the big dates providers [(4)]. With important antioxidant, antibacterial, antifungal, and antiproliferative effects, date palm fruits possess high nutritional and medicinal value. The date fruit is useful for the pharmaceutical and nutraceutical industries in the production of industrial products based on natural compounds [(5)].

1.2 Date fruits

The date has been cultivated in North Africa and the Middle East and is one of the world's most ancient fruit crops[(4)]. In many countries where they are grown, dates are the primary source of income and staple food for local people and have played a major role in the economy, culture, and climate of those countries [(6)].

In the Middle East, date fruits have been used for thousands of years as the main source of food [(3)]. Dates and their components play a role in fighting diseases through anti-oxidant, anti-inflammatory, and anti-bacterial action [(7)].

Carbohydrates are the major component of dates (44-88)%, the quality of which depends on the level of maturation and the type of dates. In addition, , dates are protein rich (2.3-5.6)%. The protein content of dates is more than that of other fruits, such as apples, bananas and oranges, where the protein content does not exceed 1% [8].

Dates contain a wide range of phenolic compounds, including p-coumaric, ferulic, sinapic acids, flavonoids, and procyanidins, many of which have anti-oxidant properties. Through the presence of anti-oxidant action, medicinal plants and their constituents play a crucial and essential function in neutralizing or inhibiting free radicals [9]. Medicinal plant constituents such as flavonoid and phenol play an important role in cancer prevention by controlling genetic processes without any side effects. The constituents of dates fruits have demonstrated anti-diseases activity as shown in Figure (1-1) [7].

Figure (1-1): Pharmalogical activities of dates fruits in diseases control [7].

1.3 Date palm cultivars grown in Iraq

In Iraq, there are over 400 date cultivars grown. They are classified into three categories based on the color and texture of the fruit: soft, semi-dry, and dry. The content of glucose, fructose, and sucrose determines the fruit type [10].

Soft dates: Soft flesh, high humidity (> 30%) and high sugar content are distinguished; the following cultivars belong to this type: Khastawi, Barhee, Halawy, Hayany and Khadrawy

Semi-dry dates: They have firm flesh, moderately low moisture (20-30%) and high sugar content; Halawi, Dayri and Khadrawy are included in this category.

Dry dates: They have a high content of sugar and low humidity (< 20 %), their flesh is dry and hard; this type includes 'Zahdi' and 'Sayer' cultivars [4] as shown in Figure (1-2).

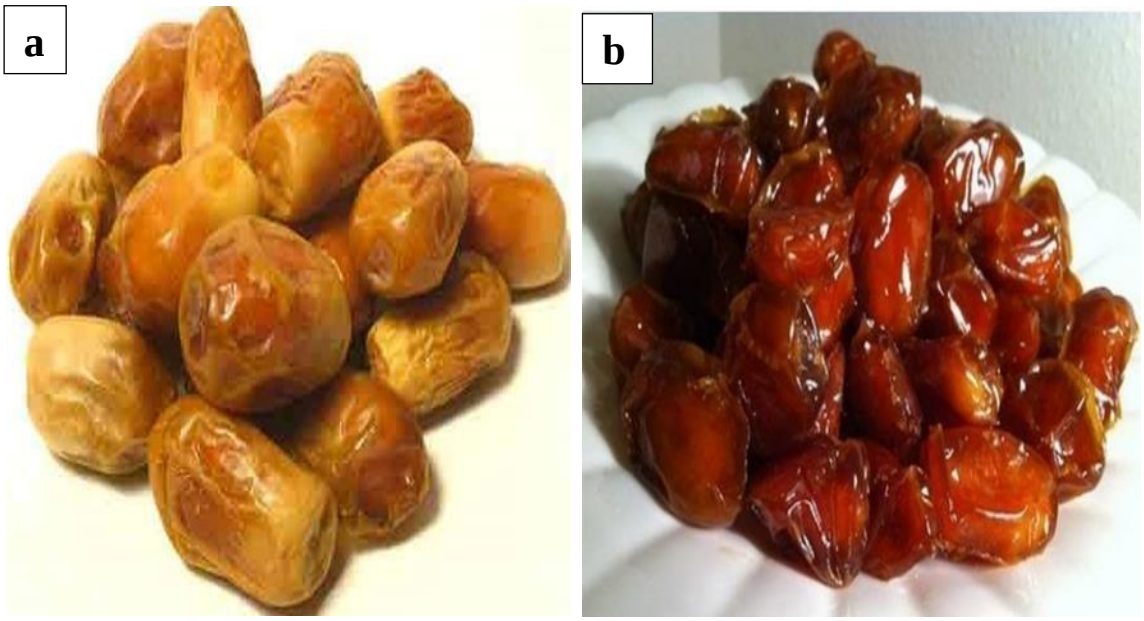


Figure (1-2): Some types of date fruit (a) Zahidi and (b) Khastawi

1.4 Nano concept

Nano is a prefix used to identify one-billionth regarding something or 10^{-9} of something [11]. In the last decade, the prefix "nano" has found an ever-increasing application to numerous fields of knowledge. The prefix derives from the ancient Greek nanus, which means essentially dwarf and by extension very small. The nanosized system is thus commonly measured in nanometers (1nm equivalent to 10^{-9} m) and it includes systems whose size is above molecular dimensions and below macroscopic ones (generally > 1 nm and < 100 nm) [12].

1.5 Nanoscience

Study of the basic concepts of molecules and structures of approximately (1-100) nm with at least one dimension. These structures are defined as nanostructures [13]. The widespread advancement in nanoscience has made it possible for nanotechnology to apply these new concepts in fields as varied as medicine, clean energy, and computing [14].

Nanoparticles are intermediate between atoms (or molecules) and bulk matter in terms of dimension. The properties of the nanoparticle vary substantially according to its size, shape, and composition. recently, advancements have been made in the biological and medicinal application of nanoparticles. The incorporation of anti-cancer agents into nanoparticles and the decoration of molecular ligand particles for cancer cell targeting, provide the possibility of more effective cancer therapy with fewer side effects. The interaction of biological molecules DNA with metallic nanoparticles enables a multitude of possible applications. One of the possible uses is as biological or chemical molecule sensors [15].

1.6 Nanotechnology

The simplest meaning of nanotechnology is technology at the nanoscale [16]. In particular, nanotechnology is distinguished as a growing and exciting one-billionth scale technology that sweeps away the boundaries between physics, chemistry, and biology. Nanotechnology is the design, characterization, manufacturing, and utilization of structures, components, and systems by regulating shape and size on a nanometer scale.

Nanotechnology has protruded as an interdisciplinary science in biomedical research that has rapidly found its own niche in clinical methodologies such as imaging, diagnosis, therapeutics, drug delivery, and tissue engineering. Nanomedicine can design, create, manipulate and optimize biological components at the nanoscale grade. This involves nanomaterial applications and the manufacturing of nano-devices for nano-diagnosis, nano-drug delivery, and drug discovery [17]. Nanotechnology is of intense importance to scientists and engineers because the basic chemical or electrical properties of materials can change at sizes below 100 nm as shown in Figure (1-3) [18].

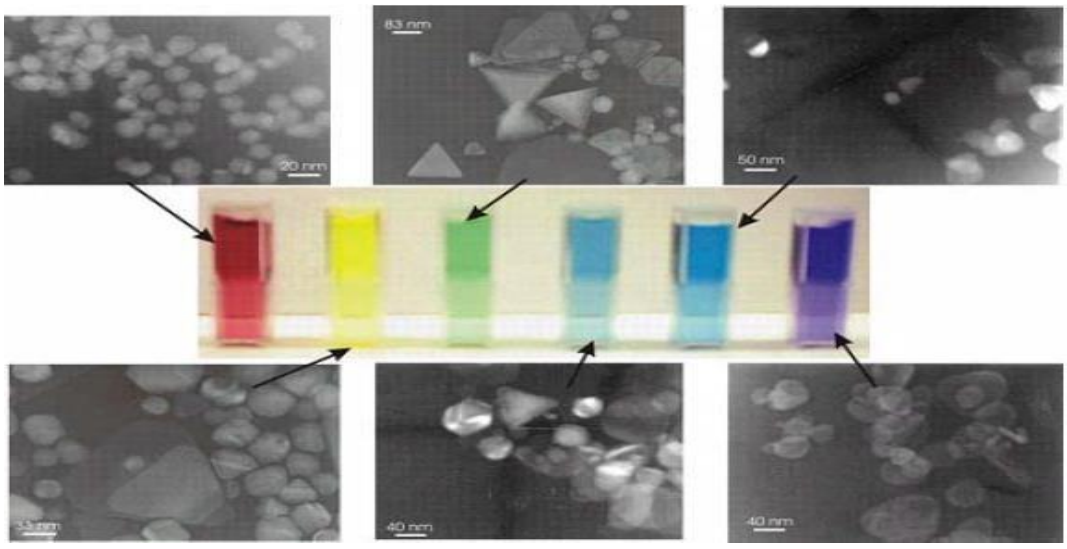


Figure (1-3): Exhibit gold nanodots in suspension the color difference is caused by particle sizes and shapes [13].

Nanoscience and nanotechnology have become significant areas of scientific research and technological advancement. Nanoscience and nanotechnology are progressing rapidly and these new areas are being connected to increasingly important social and economic prospects [19].

1.7 Applications of nanotechnology

The various fields of possible nanotechnology applications are as follows:

- **Health and medicine**:

The fields of scientific analysis have used the special features of nanomaterials for different programs (e.g., comparison providers for mobile pictures and therapeutics for the treatment of cancer). To describe this multiple field, conditions such as biomedical nanotechnology, bionanotechnology, and nanomedicine are used nanomaterials can be useful for biomedical analysis and programs both in vivo and in vitro [20].

- **Transportation:**

Like aviation lighter and stronger materials, would be useful for making vehicles that are both faster and safer. Burning engines can also benefit from components that are both more durable and more stable at high temperatures [20].

- **Energy and environment:**

The most advanced power-related nanotechnology tasks are: storage, conversion, the advancement of manufacturing through reducing materials and process speeds, power saving (e.g. by better heat-insulating material), and improved alternative power nanotechnology can add to the further decrease in the combustion of motor poisons through nanoporous channels that can clean the fumes [21,22].

- **Water and wastewater treatment:**

Materials have new size dependent properties that are distinct from their large counterparts, many of which have been tested for water and wastewater treatment applications. Some of these applications use nanomaterials scalable size dependent properties that relate to the high specific area of the surface, such as rapid dissolution, high reactivity, and sturdy sorption. Other benefits from their discontinuous properties, such as super-paramagnetism, the localized resonance of surface plasmon, and the effect of quantum confinement [(23)].

- **Food processing**

Food processing in nanotechnology, devices can be built to rapidly detect nutrient deficiencies such as atomic force microscope and the presence of pathogens in food including nanosensors. In certain food processing processes, enzymes may be used to modify food components to improve taste, nutritional value, and health benefits. The use of nanomaterials provides superior enzyme support systems (improving operation, shelf life, and cost-effectiveness) Because of their high surface to volume ratios over other macroscale support materials, they help in dispersion through food matrices [(24)].

- **Agriculture:**

Nanoparticles and materials have unequaled functional properties. There are different advantages that nanotechnologies offer, such as the higher solubility of nanoparticles in suspension, the higher surface area, and the particle size of nanoparticles, which facilitates the penetration of seed coats [(25)].

- **Electronics:**

Nanotechnology enables the development of novel optical and electronic devices, as well as novel materials for use in electronics, sensor, and catalytic technologies. Nanophysics focuses on the unique electrical and optical properties of nanomaterials, which opens up many possibilities for the construction of nanotools and nanodevices [(26)].

1.8 Nanofabrication methods

According to the processes used in constructing nanoscale structures, nanofabrication techniques may be classified loosely as bottom-up and top-down.

1.8.1 Bottom-up approaches

Bottom-up approaches of nano-fabrication aim to incorporate molecular or atomic components into more advanced nanoscale assemblies or directed self-assemblies based on complex mechanisms and technologies that enable us to monitor the development of atoms and molecules [(27)]. Atoms or small molecules are used as building blocks in this field of nanofabrication to create nanostructures that serve a variety of functions and are extremely promising for the construction of modern supramolecular architectures without generating waste or requiring the production or removal of components of the final system [(28)].

1.8.2 Top-down approaches

Top-down approaches mean starting from large pieces of material and manufacturing by mechanical or chemical methods the intended structure. Techniques that can be categorized as "Top-down" processes are crushing and milling. The top-down approach is commonly used for traditional technologies, while the bottom-up approach in nanotechnology is favored [(29)] as shown in Figure (1-4).

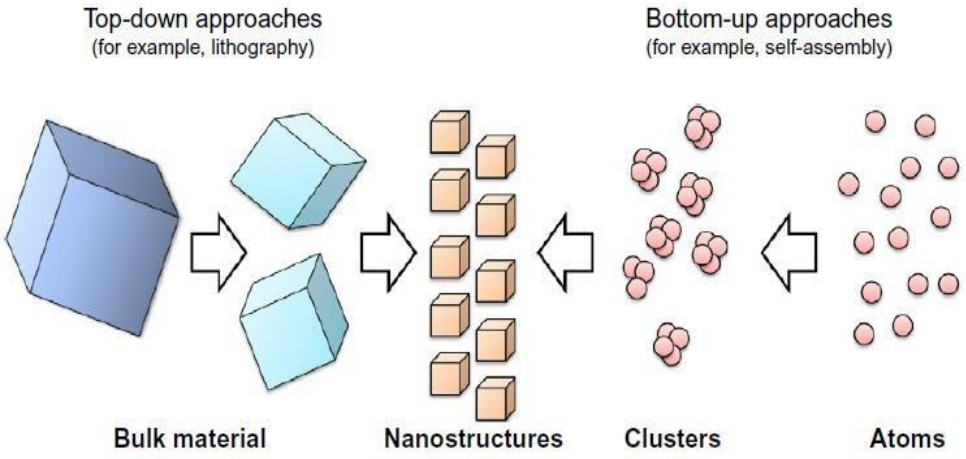


Figure (1-4): Schematic representation of bottom-up and top- down approaches for obtaining nanostructures [19].

1.9 Nanomaterials

Nanomaterials (NMs) are chemical compounds or materials made and used on a very small scale, Bulk materials are particles that are more than 100 nanometers in all dimensions. Physical properties are independent of size in bulk materials, but different physical properties can be dependent on the size and shape of nanomaterials (NMs) [30].

Nanomaterials represent an active research area and a fully expanding techno-economic strip in many fields of use. Due to their tunable physicochemical features such as melting point, wettability, electrical and thermal conductivity, catalytic activity, light absorption, and scattering, nanomaterials have gained prominence in technological advancements, resulting in improved performance over their bulk counterparts [31].

In particular, a large increase in catalytic activity is provided by the characteristic increase in surface area to volume ratio accompanying nanomaterials. The surface reactivity of nanoparticles enhances their ability to react with biological and environmental materials. Nanomaterials also allow quantum effects to regulate the behavior of the materials and have fluorescent, magnetic, and electrical capacities that are alien to their conventional chemistries [32].

Materials containing certain remarkable unique characteristics in this size range for example, crystals have a low melting point on the nanometer scale (the difference may be as high as 1000 ° C) and decreased lattice constants [33].

1.10 Types of nanomaterials

Most existing nanomaterials can be organized into two main categories [34].

1.10.1 Inorganic nanomaterials

Inorganic nanoparticles are manufactured from carbon-free materials [35].

1.10.1.1 Metal nanomaterials

Metallic nanoparticles that synthesize nanoparticles from metals such as platinum (Pt), silver (Ag), gold (Au), cadmium (Cd), cobalt (Co), iron (Fe), copper (Cu), and zinc (Zn). Such nanomaterials have unique sizes, shapes, surface areas, and densities [35]. Nanoparticles of metal ranging in size from (10-100) nm [36]. Metallic nanoparticles exhibit a wide range of physical and chemical properties in comparison to bulk metals. Metal nanoparticles, for example, displayed lower melting points, increased surface areas, unique optical properties, and unmatched mechanical power. Due to these unique properties, metal nanoparticles have a variety of important industrial applications [37]. It is used in manufacturing as a catalyst, in the electronics sector as a conductor in transistors, and in cancer detection systems. Magnetic nanoparticles have been used in a variety of fields, including cancer treatment, medication distribution, tumor detection, magnetic resonance imaging, and separation processes [38].

It can be synthesized and modified with different chemical functional groups, allowing them to be paired with anti-bodies, ligands, and drugs of interest and thereby opening up a wide variety of possible biotechnology applications [39].

1.10.1.2 Metal oxide nanomaterials

Metal oxide nanoparticles are majorly fabricated to increase their potency, reaction, and ability to change their properties. The great density and small size of corners and edges on MONPs' surfaces are responsible for their unique chemical and physical characteristics. CuO, ZnO, SnO2, Al2O3, MgO, ZrO2, AgO, TiO2, CeO2, as well as other nanoparticles, are examples. The magnetic, conductive, chemical and electronic properties of nanoparticles are all affected by their size. [40].

1.10.1.3 Ceramic nanomaterials

Ceramic nanoparticles are another term for nonmetallic solids. The ceramic nanoparticles are made by heating or cooling them repeatedly. ceramic nanoparticles may be polycrystalline, amorphous, porous, dens, or hollow ceramic nanoparticles [41]. These materials exhibited increase structural, electro-optical, superconductive, ferromagnetic, and ferroelectric properties [42].

1.10.2 Organic nanomaterials

Organic nanoparticles are solid particles built up of organic substances (often lipids or polymers) with diameters ranging from 10 nm to 1 μm [43]. Organic nanoparticles with interesting properties have gotten a lot of attention in the scientific community for applications including disease diagnostics, drug delivery, bio imaging, and cancer treatment [44]. involve Carbon-based nanoparticle These nanomaterials are found in morphologies such as hollow tubes, ellipsoids, or spheres. Fullerenes (C60), carbon nanotubes (CNTs), carbon nanofibers, carbon black, graphene (Gr), and are exceedingly used in biomedical

applications [34]. Organic or polymeric nanomaterials, such as dendrimers micelles, liposomes, and nanogels, are attractive building blocks for multifunctional. Due to their flexible surface and core chemistry, high degree of biodegradability, efficient endocytosis by the target cell, and high loading capacity [45].

1.11 Classification of nanomaterials

Nanomaterials contain a wide variety of materials that can be prepared mechanically, chemically, physically, or naturally and have a size in the nanoscale range. various Nanomaterials structures are generally determined by their dimensions [46]. Nanomaterials are classified into four types: zero-dimensional, one-dimensional, two-dimensional, and three-dimensional, as shown in Figure (1 -6) [47].

1.11.1 Zero-dimensional nanostructures (0D)

Nanomaterials belong to this class because all of their dimensions are in nanoscale, which means they must be smaller than 100 nm. Spherical shaped materials are typical nanomaterials in this group, but this class can also include cubes, nanorods, and polygon shaped nanostructures. Holospheres, noble metal nanoparticles, metal/metal oxide nanoparticles, core-shell nanomaterials, quantum dots, are some instances of this class in general [46].

1.11.2 One-dimensional nanostructures (1D)

The materials that are confined in two dimensions but free in one dimension are one dimensional nanomaterials. Wires, nanowires, nanotubes, nanofibres, nanobelts, nanoribbons, nanorods, and hierarchical nanostructures are some of the typical examples of 1D nanomaterials.

Because of their extraordinary properties and broader applicability in research and development and material development, such nanomaterials have acquired tremendous considerations. These materials have a broader impact on nanoelectronics, nano-devices, and systems [48].

1.11.3 Two-dimensional nanostructures (2D)

Nanostructures with two dimensions above the nanoscale and one dimension in the nanoscale range fall into this group. Two-dimensional nanomaterials may be single or multilayered crystalline or amorphous metallic, ceramic, or polymeric layers deposited on a substrate with a variety of chemical configurations [49].

1.11.4 Three-dimensional nanostructures (3D)

Three dimensional nanomaterials are such materials that in all three directions have their free dimensions and there are no restrictions and limitations. Powders, multilayers, fibrous, and polycrystalline materials are typical examples of three dimensional nanomaterials.

The three dimensional nanomaterials have a broad specific surface area and offer sufficient surface adsorption sites for molecules in a small area owing to these nanostructures. Nanomaterials with three dimensions are commonly used in catalysis, magnetism, and the development of electrode materials for batteries [48].

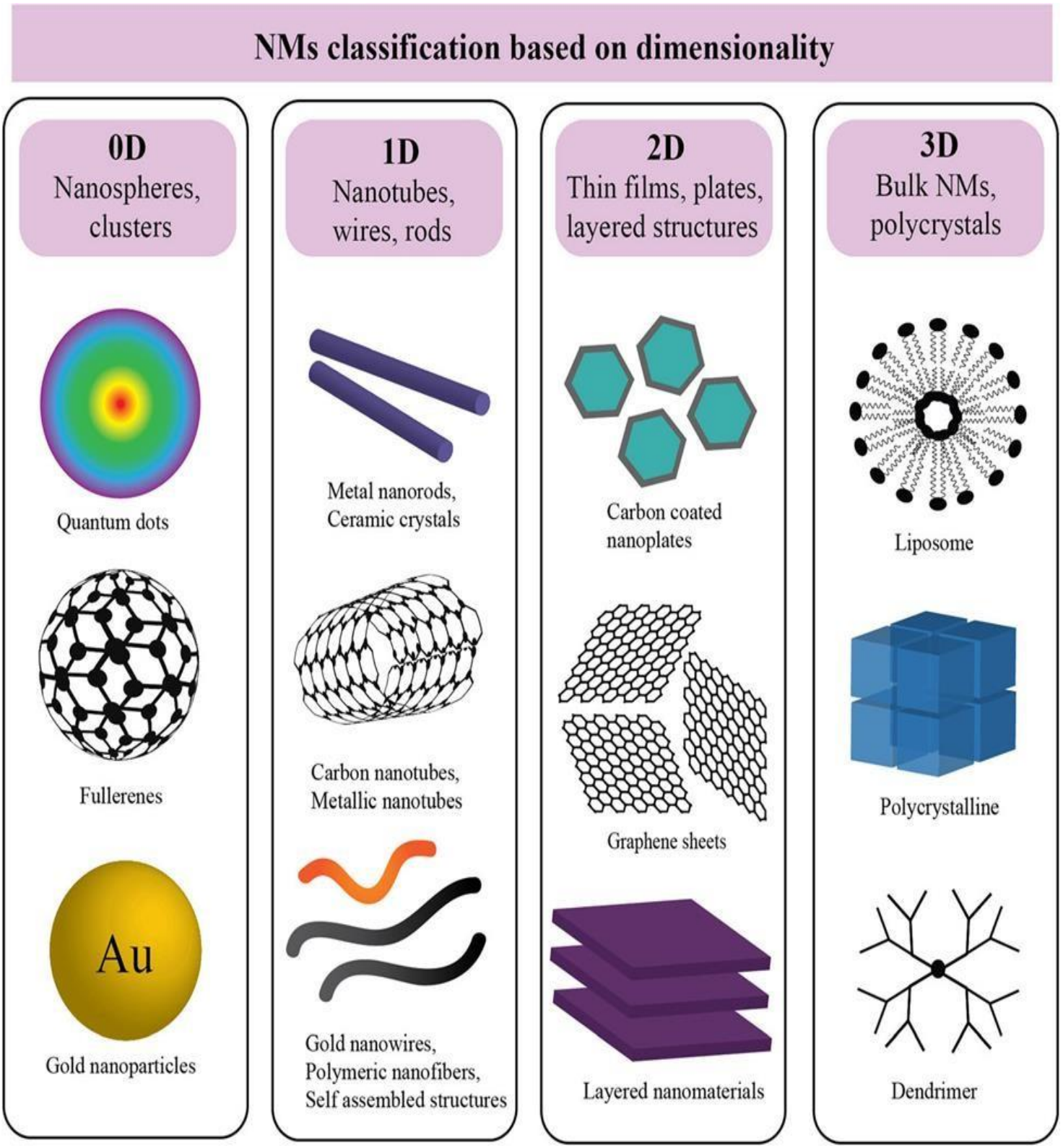


Figure (1-5): Schematic impersonation of the classification nanomaterials on the base of their dimensions [47].

1.12 Nanomaterial synthesis methods

Methods commonly used for the synthesis of nanomaterials are as follows [50]:

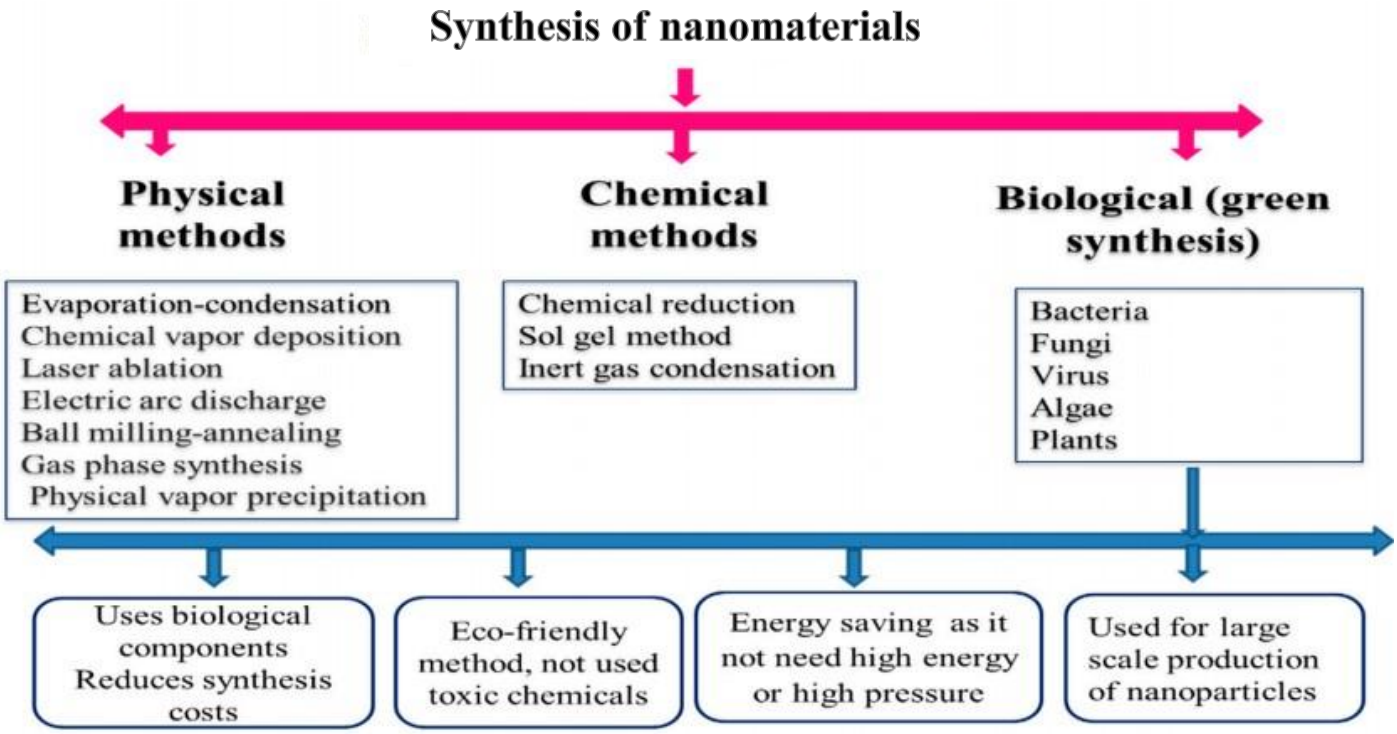


Figure (1-6): Different available nanofabrication methods for the preparation of nanomaterials [50].

1.12.1 Physical methods

Physical nanoparticle synthesis methods include UV irradiation, sonochemistry, laser ablation and radiolysis, etc. Evaporation of metal atoms happens during the physical synthesis process, accompanied by condensate on different supports, where the metal atoms are rearranged and aggregated as small clusters of metallic nanoparticles. Nanoparticles can be synthesized with a high purity and definite form using physical approaches. These methods, on the other hand, often necessitate highly advanced instruments, chemicals, and radiative heating, as well as high power consumption that resulting in high running costs [50].

1.12.2 Chemical methods

The majority of chemical approaches used to synthesize nanoparticles are focused on reduction processes. Since they need a precursor (a molecule containing metal atoms whose nanoparticle would be produced) dissolved in a solvent and a reduction agent, alkali metal borohydrides, such as sodium borohydride ($NaBH_4$), are among the inorganic reductants [51].

The chemical approach entails the use of toxic substances that can be hazardous to the ecosystem as well as the individual handling them [52].The chemical method includes poisonous solvents, high pressure, energy, and high temperature to prepare nanoparticles [53]. Reducing agents used to reduce metal ions and stabilizing agents used to avoid undesired agglomeration of the nanoparticles formed in conventional chemical and physical methods both pose a risk of toxicity to the environment and the cell. Furthermore, the contents of the nanoparticles formed are thought to be toxic due to their shape, size, and surface chemistry [54].

1.12.3 Biological methods

Biological nanoparticle synthesis is a green chemistry technique that interconnects between nanotechnology and biotechnology [55]. Green chemistry was applied to the nanoparticles synthesis technique to reduce toxic materials and to minimize the production of unwanted or toxic byproducts. The organic synthesis of nanoparticles using plant extracts is known as green nanotechnology or green synthesis, and the synthesized nanoparticles are known as biogenic nanoparticles [56].

Green synthesis is a superior, simple, eco-friendly, biocompatible, biodegradable, non-toxic, and cost-effective approach to nanoparticle synthesis. It is based on a variety of green plant extract sources that stabilize/capped or reduce or both the nanoparticles [57].

Greener nanoparticle synthesis is superior to other methods because it is simple, cost-effective, and relatively repeatable, as well as producing more stable materials [58].

Microorganisms may also be used to generate nanoparticles, however, the pace of synthesis is sluggish and only a small range of sizes and shapes are amenable to the method compared to routes involving plant-based materials. There is no need for high pressure, energy, temperature, or harmful chemicals in the green synthesis process. As a result, many researchers are moving away from synthetic methods these days. Plants generate more stable nanoparticles than other methods and it is very easy to scale up. A hazard of contamination is also less likely [59].

Plant extracts include a range of bioactive substances, such as alkaloids, proteins, phenolic acids, carbohydrates, terpenoids, and polyphenols as shown in Figure (1-8).

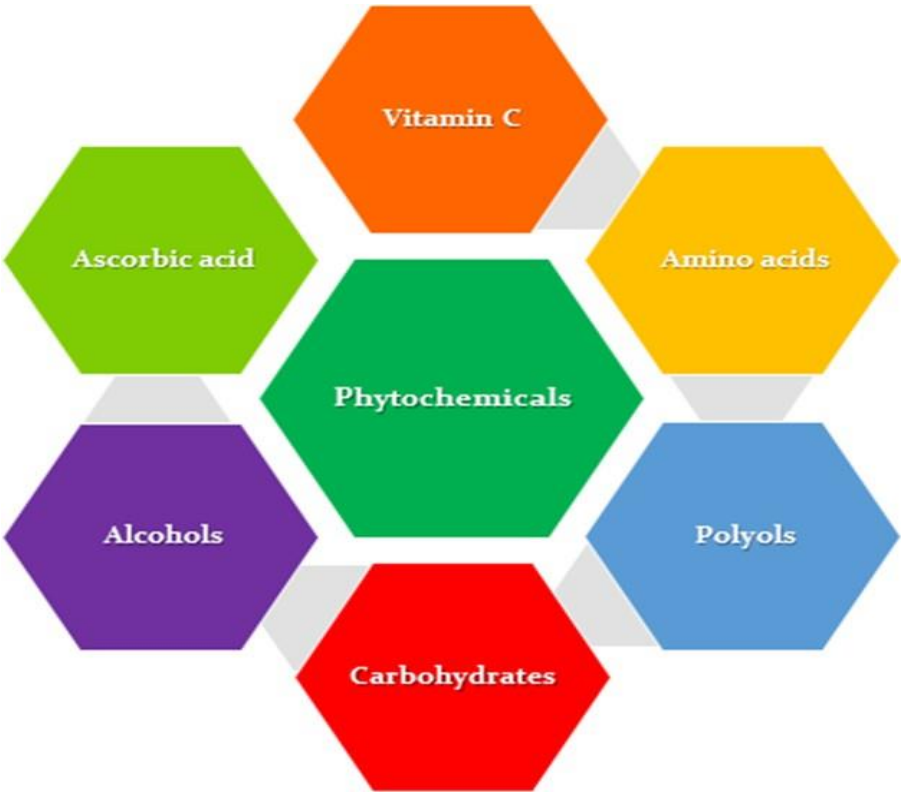


Figure (1-7): Significant bioactive components found in plant extracts [58].

Many of which have been shown to succeed in the reduction and stabilization of metallic ions as shown in Figure (1-9) [60].

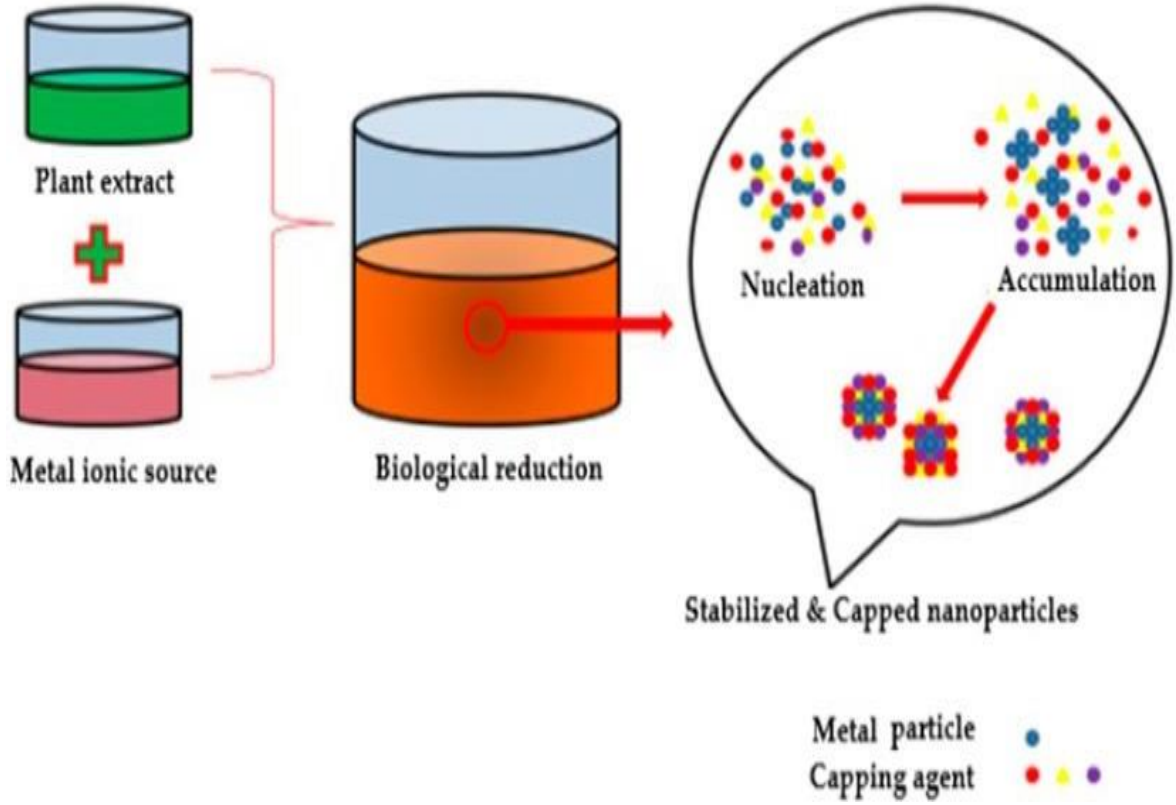


Figure (1-8) Biological synthesis of nanoparticles by using plant extracts [60].

1.13 Platinum

Platinum (Pt) is one of the scarce elements in the Earth's crust. It's a scarce special precious metal that's a strategic commodity for industries in many countries. Platinum is dense, malleable, ductile, and silvery-white Figure (1-10). The noun platinum comes from the Spanish word Platina, which means "little silver." There are six natural isotopes of platinum: ^{190}Pt, ^{192}Pt, ^{194}Pt, ^{195}Pt, ^{196}Pt, and ^{198}Pt, the ^{195}Pt is being the most plentiful [61].

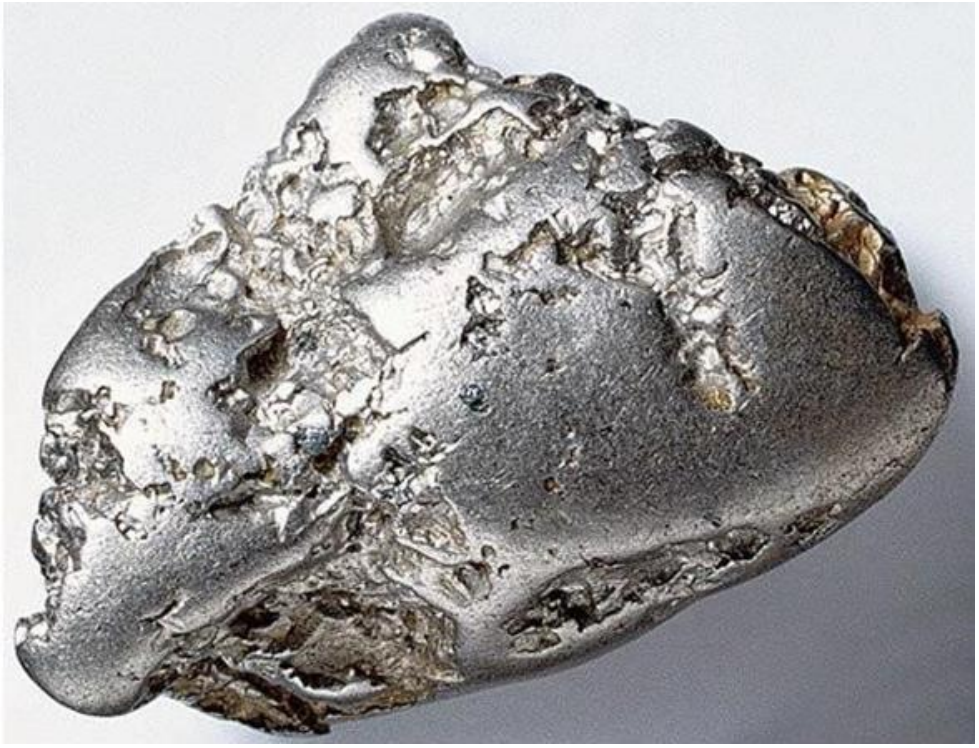


Figure (1-9): Image of platinum in row form [61].

1.13.1 Physical and chemical properties of platinum

Platinum is a silvery-white metal that belongs to the periodic table's sixth period. Platinum has remarkable physical and chemical properties, including high melting points, corrosion-resistant, and catalytic properties[62]. Their chemical stability, oxidation resistance, and mechanical properties at extremely high temperatures are the most significant characteristics [63].

In an aqueous solution, the most typical oxidation state of Pt is either the +2 or +4 valence state. At 25°C, the divalent state dominates the tetravalent state, with the exception of highly oxidizing conditions [64].

Table (1-1): Physical and chemical properties of platinum [61] .

Property	Value
Formula	Pt
Color	silvery white
Atomic number	78
Atomic mass	195.08 g/mol
Atomic radius	1.377 A˚
Crystal structure	Face cubic center (fcc)
Density (20°C), g/cm^3	21.45 g/cm^3
Melting point	1772 °C
Boiling point	3827 °C

1.13.2 Uses of platinum

Platinum is used in a number of uses, due to its special properties, including: high mechanical efficiency, electrical conductivity, catalytic activity, inertness, and biocompatibility. Platinum is becoming more common in medical manufacture. One of the most distinguished properties of platinum is its capacity to prevent living cells from dividing. Among the first Pt-based anti-cancer drugs to be discovered include cisplatin, carboplatin, oxaliplatin, picoplatin, and satraplatin[65].

Because of its relative inertness and stability in biological environments, platinum (Pt) has been widely used in medical electrodes. The size of implantable therapeutic devices is becoming smaller and smaller [66]. Platinum electrode (Pt) is a suitable candidate because of its strong electrical conductivity and corrosion resistance. Platinum has been successfully used in a variety of areas, including fuel cells and organic compound oxidation [67]. Platinum is also mainly used in the glass, electrical, electronics, and petroleum industries, as well as jewelry manufacturing and dental alloys [68].

1.14 Platinum nanoparticles (PtNPs)

Platinum nanoparticles (PtNPs) are sometimes in the form of a suspension or colloid of nanoparticles of platinum in totally fluid, sometimes water. A colloid is a stable dispersion of particles in a very fluid medium, as described by science (liquid or gas). Depending on reaction conditions, spherical noble metal NPs with sizes ranging from (2 -100) nm will be generated. PtNPs are suspended in a maroon or black-colored colloid. Nanoparticles are obtainable in a variety of shapes, including spheres, rods, cubes, and tetrahedral shapes. PtNPs are now the subject of extensive research, with possible uses in a wide range of fields. As a result, the chemical alteration, medicine, and the synthesis of new materials with distinct properties are all covered [(69)].

Platinum nanoparticles are widely used in a variety of technologies, including consumer products cosmetics, supplements, food additives, electrocatalysis, data storage systems, new electronic devices, electrochemical biosensors, chemosensors, fluorescent and refract metric sensors, as well as medicine, diagnostics, and treatment, due to their lower cytotoxicity caused by chemical stabilization and resistance to ionization, as compared with other metal nanoparticles. Platinum nanoparticles (PtNPs) have a variety of biomedical uses, including surgical devices, drug delivery vehicles, and photothermal therapy compounds, as well as improved radiosensitization, cancer cell identification, tooth structure bond strength, and bacterio-toxic effects [(70)].

1.15 Properties of platinum nanoparticles

Due to their unusual and tunable surface plasmon resonance (SPR), platinum nanoparticles have been considered a significant field of study [(71)]. Platinum nanoparticles have a plasmonic property in the UV-Visible range and their heat generation efficiency is higher than that of other nanometals [(72)].

Platinum nanoparticles are required to reduce the role of reactive oxygen species (ROS) .Platinum nanoparticles in medicine capable of quenching superoxide anion and hydrogen peroxide [73]. Because of their special crystalline, optical, and catalytic properties, platinum nanoparticles are particularly exploited for catalysis and biomedical applications. They may function as nanoenzymes, nanocarriers, and nanodiagnostic tools [74].

1.16 Applications platinum nanoparticles

Platinum nanoparticles are used in a variety of areas, including chemistry, medicine, electronics, and biology. Nanoparticle applications primarily depend on their size, shape, morphology, and dispersion [75].

1.16.1 Fuel cell catalyst

Platinum is used as a catalyst in anode and cathode reactions.

Due to their superior catalytic activity, stability, and selectivity, platinum nanoparticles are favored over other metallic membrane fuel cell catalysts. Furthermore, various platinum nanoparticle synthesis strategies are being explored in order to ensure their direct use as an electro-catalyst in methanol fuel cells [76].

1.16.2 Catalytic converters

Because of their significant industrial uses, such as the removal of pollutant gases from vehicles, platinum nanoparticles have been studied extensively in the field of catalysis. The catalytic reactivity of platinum nanoparticles is strongly dependent on particle morphology [77].

1.16.3 Electrochemical sensor

Electrochemical sensors have a high sensitivity, excellent stability, are simple to use, and inexpensive. Because of their important catalytic and optical activities, platinum nanoparticles are extensively used in electrochemical sensors [76].

1.16.4 Glucose detection

Biosensors based on glucose enzymes have been shown to be effective in a variety of applications, including medical diagnosis, bioprocess tracking, beverage industry monitoring, and environmental monitoring. A highly sensitive glucose enzyme sensor based on platinum nanoparticles [78].

For electrochemical glucose detection, the $Pd_85Cu_9Pt_6$ trimetallic nanocrystals have high catalytic activity and selectivity. These trimetallic catalysts have the potential to be useful in medical applications such as blood glucose sensing, as well as ecological approaches, and environmental monitoring [79].

1.16.5 Cancer therapy

1.16.5.1 Chemical cancer treatment

Platinum nanoparticles can scavenge H_2O_2 and $O_2^{\bullet}$, which reduce oxidative stress in cells that activates anti-inflammatory responses that guard against inflammation and disease caused by inflammation. Platinum nanoparticles have been shown to shield keratinocytes from UV-induced inflammation by limiting the generation of reactive oxygen species (ROS) and preventing apoptosis[80].

Platinum nanoparticles exhibited effective lethality against the cancer cells that were effectively killed. Both in vitro and in vivo anti-tumor effects results were estimated and showed excellent therapeutic efficacy [81].

The ability of platinum nanoparticles to penetrate cells has been shown. There is also a proof of DNA damage and anti-oxidant response alteration associated with platinum nanoparticle treatment in vitro. Platinum ions derived from nanoparticles may then be used to treat cancer in a similar way to cisplatin [82].

1.16.5.2 Photothermal therapy and radiotherapy

Metal nanostructures are promising photothermal therapy (PTT) and radiotherapy (RT) agents that enhance cancer management techniques by sensitizing to laser light and X-ray.

In nanomedicine, nanoscale platinum materials are advantageous as metallic nanostructures are used as radiosensitizers. They increase X-ray absorption and enhance radiotherapy efficacy. Metallic nanostructures promising benefits contribute to dose enhancement [83].

1.16.6 Antibacterial agent

Platinum nanoparticles cause bacterial growth inhibition by inhibiting ATP-dependent protein synthesis and inducing DNA destruction [84]. Membrane damage occurs as nanomaterials bind electrostatically to the bacterial cell wall and membranes resulting in a change in membrane potential causing an imbalance of transport, disrupted respiration, obstruction of energy transduction, cell lysis, and ultimately cell death [85].

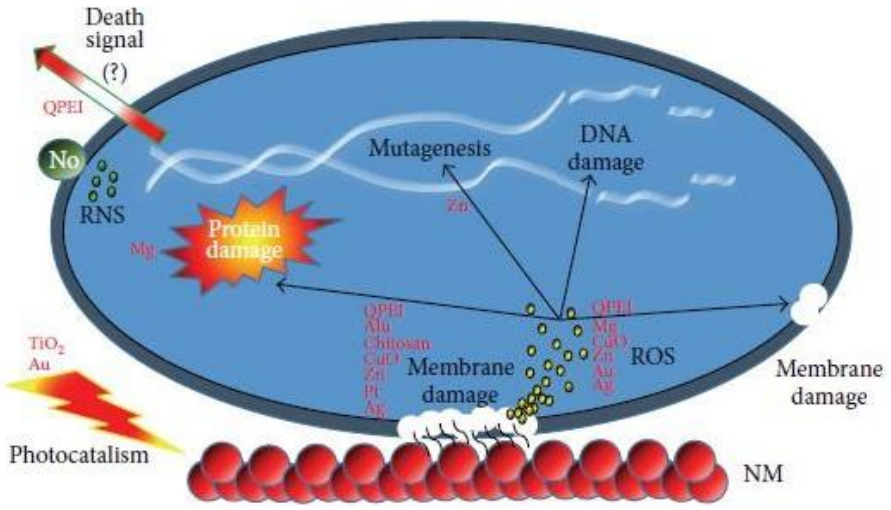


Figure (1-10): Mechanism of nanomaterial entry into the bacteria cell [85].

1.17 Cancer

Cancer is a term used to describe diseases in which cells divide abnormally and without regulation. This unregulated division results in the formation of a lump called a tumor, or rogue immune system cells to develop, invasion of other tissues, and prevalence to other parts of the body across blood vessels and lymph systems. There are over 100 distinct cancer types, most of which are named for the location in the body where cancer first originated or the type of tissue cell in which they begin/originate [86].

Cancer disrupts cellular relationships and causes essential genes to malfunction. This disruption has an impact on the cell cycle, resulting in abnormal proliferation. Different stages of cancer were identified, suggesting that multiple gene mutations play a role in cancer pathogenesis. Pathological cell proliferation is caused by these gene mutations. Genetic defects resulting from inheritance factors play a critical role in cell growth [87].

Cells develop into cancer cells as a result of DNA disruption, and subsequent cells would all have the same affected DNA as the initial cell. In the majority of cases, cancer cells produce a tumor. A malignant tumor is a collection of cancer cells that may invade surrounding tissues or spread to other parts of the body. Tumors are not all cancerous. Non-cancerous tumors are referred to as benign tumors. Benign tumors may get very large and push on healthy organs and tissues, causing complications. However, they cannot penetrate (grow into) other tissues. They can't spread to other areas of the body so they can't invade (metastasize). Almost none of these cancers are life-threatening [88].

Corona virus disease - 2019 (COVID-19) is associated with a high risk of death in cancer patients. Appropriate and aggressive prevention steps must be taken to mitigate the risk of SARS-CoV-2 infection in cancer patients, as well as to best treat those who have become infected [89].

1.17.1 Causes of cancer

There are a variety of reasons that contribute to the development of cancer [90].

1.17.1.1 Endogenous causes

Inherited germ line mutations: Germline mutations are genetic changes that are passed on from egg or sperm DNA. Inherited germline mutations do not guarantee cancer, but they do increase the risk of developing cancer as compared to the general population[90].

Oxidative stress: The reactive oxygen species produced by normal oxidative metabolism have the potential to damage DNA extensively [90].

Inflammation: Is a natural reaction to bacteria, foreign bodies, trauma, chemicals, and Chronic inflammation, that can damage DNA and promote cancer [91].

Hormones: Exposure to estrogen over a lifetime increases the likelihood of breast, ovarian, and endometrial cancers in women, and can be a source of these cancers [92].

1.17.1.2 Exogenous causes

Tobacco use: Tobacco use leads to cancer deaths and smokers are at a higher risk of developing a variety of cancers. Tobacco smoke causes lung cancer in both men and women [93].

Infectious agents: Such as viruses, bacteria, and parasites may cause DNA damage and contribute to the growth of cancer [93].

Radiation: Ionizing and UV radiation both cause DNA damage and carcinogens. This covers the radiation used in X-ray radiographs as well as cancer therapy[94].

Medication: A variety of surgical treatments can reduce the risk of some tumors. X-rays, as well as radiation used to cure cancer, are both carcinogenic[94].

Industrial chemicals: Certain manufacturing chemicals and insecticides remain in the ecosystem and accumulate in the food chain [95].

Food containing carcinogens: Natural or man-made carcinogenic toxicants can contaminate food. Molds and the contaminants released by certain molds are carcinogenic and cause DNA adducts [96] as shown in Figure (1-12).

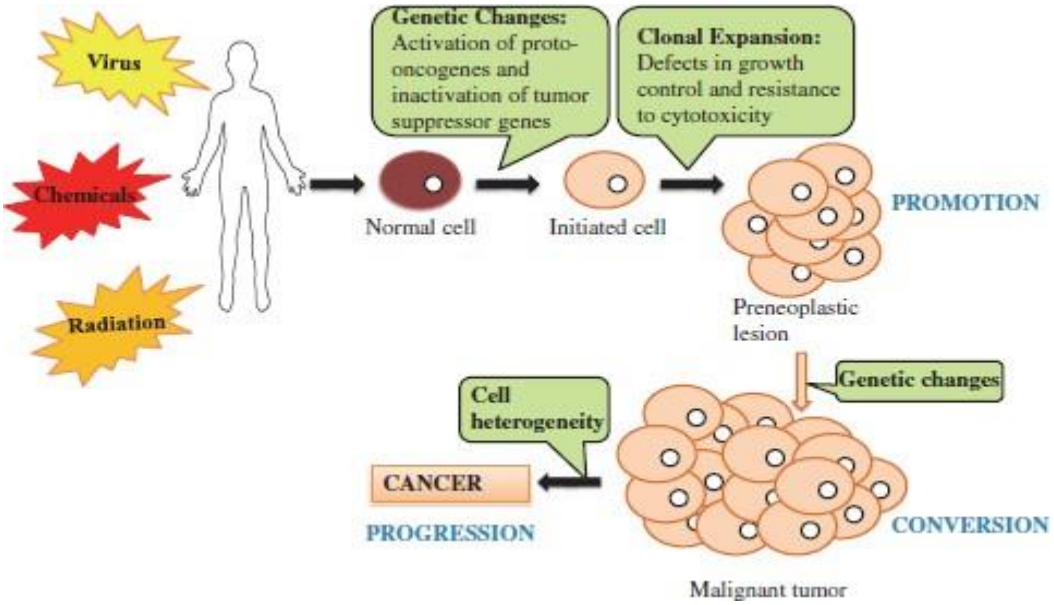


Figure (1-11): Most of the causes of cancer and how cells turn into cancer cells [93].

1.17.2 Categories of cancer

Cell tissue tumors can be divided into types based on the type of cell tissue in which they begin [97].

- **Carcinomas**: The skin or the tissue that protects the surface of internal organs and glands is where carcinoma starts. Carcinomas are usually solid tumors. Cancers of this kind are the most widespread. Prostate cancer, breast cancer, lung cancer, and colorectal cancer are examples of carcinomas [97].
- **Sarcomas**: Sarcomas begin in the body is supporting and connecting tissues. Sarcomas can appear in the fat, muscles, nerves, tendons, joints, blood vessels, lymph vessels, cartilage, or bone [97].
- **Leukemia**: Is a blood cancer. When healthy blood cells start to change and expand uncontrollably, leukemia develops. Acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, and chronic myeloid leukemia are the four primary forms of leukemia [97].
- **Lymphomas**: Lymphoma is cancer that starts in the lymphatic system and spreads across the body. The lymphatic system is a set of vessels and glands that aid in the fight against infection. Lymphoma is divided into two types: Non-Hodgkin lymphoma and Hodgkin lymphoma [97].
- **Myeloma** (plasma cell myeloma) : Is a blood cancer characterized by the clonal proliferation of malignant plasma cells [98].

  Multiple myeloma (MM) is a B-cell malignancy characterized by the aggregation of malignant plasma cells in the bone marrow [99]. The tumor cells spread across the bone marrow (BM), causing "pancytopenia" and "osteolytic" bone devastation [100].

1.17.3 Treatment methods [101].

Surgery: Is commonly used to cure cancer that is localized, and it can be used to eliminate only the main portion of the tumor .

Radiation therapy: High-energy X-rays are used in radiation therapy to destroy cancer cells .

Chemotherapy: Is a form of cancer treatment that involves the administration of anti-cancer drugs through a vein or by mouth .

Hormone therapy: Many breast cancers are developing by estrogen, a hormone produced by the ovaries in women. Androgens (male sex hormones) including testosterone, which is produced by the testicles, also stimulate the development of most prostate cancers .

1.18 Ovarian cancer

Ovarian carcinomas are a diverse group of tumors that are traditionally divided into subtypes based on the type and degree of differentiation [(102)]. There are three forms of ovarian cancer: Epithelial (the most common), Germ cell, and Sex cord stromal [(103)].

Ovarian epithelial tumors are a variety of tumors. The most common and lethal gynecological malignancies are malignant epithelial tumors (carcinomas). Ovarian carcinomas are classified into five groups based on histopathology and molecular genetic alterations: high-grade serous (70%), endometrioid (10%), clear cell (10%), mucinous (3%), and low-grade serous carcinomas (5%),none of these cells are present in the normal ovary [(104)].

1.18.1 Symptoms

Lower abdominal pain ambiguous and nonspecific. Anorexia, bloating, abdominal and pelvic discomfort urination urgency frequency, weight reduction, pelvic pain, changes in bowel behavior like constipation ovarian cancer may be discovered by mistake during surgery for other reasons or during examinations [(105)].

1.18.2 Treatment methods

Ovarian cancer has the highest mortality rate. of all gynecological cancers, the mainstays of treatment are cytoreductive surgery and adjuvant chemotherapy [106]. Enucleation surgery and chemotherapy are used to treat women [105].

1.19 Oesophageal cancer

Oesophageal cancer is one of the most common cancers and a major cause of death from cancer. The disease is highly active, with a weak diagnosis [107]. It is the ninth most prevalent cancer worldwide and the sixth leading cause of death from cancer. This cancer has a long list of care requirements [108].

Squamous cell carcinoma and adenocarcinoma, two forms of oesophageal cancer, have different risk factor profiles. The key risk factors of oesophageal squamous cell carcinoma are cigarette smoke and excessive alcohol consumption. Gastro oesophageal reflux disease (GORD) and obesity are the major risk factors for adenocarcinoma, while cigarette smoking is a relatively strong risk factor for both types of oesophageal cancer. Dietary factors can affect the risk of both types of oesophageal cancer. While genetic factors play a role in the etiology, but their impact is usually minor [109].

1.19.1 Symptoms

Dysphagia (pain in swallowing food and liquids) affects the majority of patients with oesophageal cancer. Weight loss consistent indigestion, heartburn, or reflux of food. Pain or discomfort in the upper tummy, chest, or back [110].

1.19.2 Treatment methods

Oesophageal and gastric cancer surgery are excellent examples of complex procedures which can be associated with significant weight loss, malnutrition, and sarcopenia. In the current century, surgery is preceded by either chemotherapy or a combination of chemotherapy and radiotherapy for the majority of patients who present with locally advanced disease [111]. Chemotherapy and radiation therapy, followed by surgical resection or without surgical resection, are examples of multimodal therapy [112].

1.20 Bacteria

Bacteria are prokaryotic cells that are in general the size of mitochondria. Their length ranges from 0.2 to more than 10 μm, and their width ranges from 0.2 to 1.5 μm. Under a light microscope, a multitude of bacterial shapes can be seen, including cocci, rods, spirals, and even cubes. Scanning electron microscopy (SEM), which offers a three-dimensional image of cellular structures as well as information about their surface topography, may also reveal these shapes. Bacteria can be classified into two types: Gram-negative bacteria and Gram-positive bacteria. It is possible to investigate the ultrastructural variations between Gram-negative and Gram-positive cell walls. Understanding the chemical composition of the cell wall is important [113,114].

1.20.1 Gram-negative cell walls

Gram-negative cell wall is composed of an external membrane overlying an inner peptidoglycan layer [115].

1.20.2 Gram-positive cell walls

The Gram-positive cell wall, different from its Gram-negative equivalent, lack an outer membrane but has a larger peptidoglycan layer [115].

Infections including strep throat and foodborne diseases are caused by bacteria. Antibiotics are medications that are used to cure bacterial infections [114].

1.21 *Pseudomonas*

Pseudomonas species are Gram-negative, aerobic, non-spore-forming rods that are straight or mildly bent and measuring (0.5–1.0) μm by (1.5–5.0) μm. They are motile using one or two polar flagella. They have a rather strict aerobic respiratory metabolism with oxygen, but nitrate is used as a substitute in some cases to enable anaerobic growth [116].

Pseudomonas is a large and widespread bacterial genus that can be found in a wide range of niches and environments. It is the highest number of recognized species. There have been over 220 species identified. *Pseudomonas aeruginosa, Pseudomonas fluorescent, and Pseudomonas* pertucinogena are members of three major lineages dependent on the sequences of the 16S rRNA gene [117].

Pseudomonas species, in general, grow quickly and are known for their ability to metabolize a wide range of substrates, including toxic organic chemicals like aliphatic and aromatic hydrocarbons. *Pseudomonas* strains are often resistant to antibiotics, disinfectants, detergents, heavy metals, and organic solvents [118].

1.22 *Pseudomonas aeruginosa*

Pseudomonas aeruginosa (*P. aeruginosa*) is a bacterium that belongs to the Pseudomonadaceae , which is a representative of a Gammaproteobacteria family. It is a non-sporulating Gram-negative organism with a length of (1-5) μm and a width of (0.5-1) μm. It has a polar monotrichous flagellum that allows it to move in liquid media and on solid surfaces. *P. aeruginosa* is a mesophilic bacterium that can grow

in temperatures ranging from (4 – 42) °C, and can be present in a pH range of 4.5 - 9.5 in both watery and overland environments [119].

Pseudomonas aeruginosa can grow anaerobically and does not ferment, instead obtaining energy from sugar oxidation. It can grow in a variety of environments, including dry surfaces in hospital operating rooms, hospital rooms, clinics, and medical equipment, as well as sinks, showers, and even contaminating distilled water, and has thus been identified as a significant source of nosocomial infection[120].

Pseudomonas aeruginosa is a bacteria that can affect people with compromised natural defenses and cause extreme pulmonary disease[121]. In patients with nosocomial bloodstream infection, *P. aeruginosa* is the fifth most prevalent nosocomial pathogen.

Clinical manifestations include infections that are mostly nosocomial or healthcare-associated, such as pneumonia (the second most frequent cause of nosocomial pneumonia), urinary infections, surgical wound infections, bone, and joint infections, and bloodstream infection, but also infections that are commonly acquired in the community, such as gastrointestinal infections, skin, soft tissue infections, bacterial keratitis, and "malignant" otitis externa [122].

1.23 *Streptococcus*

Streptococcus belong to the Streptococcaceae family that includes the genera Streptococcus, Lactococcus, and Lactovum . When grown in liquid media, Strains of Streptococcus are usually spherical or ovoid in shape .They have a diameter of less than 2μm and are found in chains or pairs. Gram-negative cells are immobile and do not form endospores. Cell wall contains the diamino acid lysine. Almost all species are facultatively anaerobic, but some do need additional CO_2 to grow. [123].

The optimal temperature is usually about 37°C, but depending on the species, the maximum and minimum temperatures vary. Many organisms

live as commensals or parasites on humans and animals, and some are particularly pathogenic. A capital letter of the alphabet is assigned to each strain (A, B, C, E, F, G, etc) It is particularly useful for distinguishing between human and animal infections caused by β-hemolytic streptococci[124] .

Streptococci are one of the most common bacteria that colonize the human respiratory tract. *Streptococcus pyogenes* is one of these strains of a human pathogen. It is a significant source of morbidity and mortality in humans all over the world. Group A streptococci (GAS) cause 18 million cases of serious disease and many deaths per year [125].

1.24 *Streptococcus pyogenes*

Streptococcus pyogenes (group A beta-hemolytic streptococcus) is Gram-positive and catalase-negative coccus. It can be found asymptomatically in the pharynx, skin, vaginal canal, and rectum.There is a broad diversity of clinical presentation of group A beta-hemolytic streptococcus (GAS). While the most common GAS infections are mild (e.g., pharyngitis and skin infections), if left unchecked, severe secondary effects such as rheumatic fever and glomerular nephritis may arise [126].

GAS diseases include a wide range of pathogens, including localized and systemic infections that can cause acute or chronic illness [127].

1.25 Literature review

The literature review includes several papers that bind platinum nanoparticles with biological applications by using biological approaches in synthesis.

Sadeeq Ullah, *et.al*. [128] studied the use of phytochemicals in the aqueous extract of *Maytenus royleanus* that used to reduce Pt ions into PtNPs. The study revealed that biogenic PtNPs have anticancer activity in vitro against the lung cancer cell line (A549). Importantly, the as-prepared Pt NPs were well tolerated by normal human cells, and therefore, could be effective and biocompatible agents in the treatment of different cancer cells.

Tahir, K., *et.al*. [129] used the biomolecules of plant extract of *Taraxacum laevigatum* as a reduction and capping factor for the synthesis of small and spherical platinum nanoparticles. PtNPs showed inhibition zones against the activity of two bacterial species *B. subtilis* and *P. aeruginosa.*

Rokade, S., *et.al*. [130] prepared the platinum nanoparticles (PtNPs) and palladium nanoparticles (PdNPs) using *Barleria prionitis* leaf extract (BPLE). The bioreduced nanoparticles were monodispersed, extremely small and stable against human breast adenocarcinoma (MCF-7) cell lines, the particles showed potent anti-cancer activity. The treatment of cells with PtNPs and PdNPs significantly reduced their viability.

Ramkumar, V., *et.al*. [131] studied synthesis of PtNPs using aqueous extract of Indian brown seaweed *Padina gymnospora* and their catalytic activity with a polymer Polyvinylpyrrolidone (PVP) as PVP/PtNPs nanocomposite. The aqueous extract could be seen as an efficient reducing and capping factor for the biosynthesis of the PtNPs. Anti-bacterial activity against disease-causing pathogenic bacterial strains with the

highest activity against *Escherichia coli* followed by *Lactococcus lactis* and *Klebsiella pneumoniae*.

Jeyapaul, U., *et.al*. [132] produced PtNPs and PdNPs by using Gloriosa Superba tuber extract that was identified to be almost isodiametric and uniformly spherical. The synthesis was fast, effective, and safe for the environment. against MCF-7 (human breast adenocarcinoma) cells, both Pt and PdNPs demonstrated potent anti-cancer activity. Studies on these phytogenic nanoparticles can aid in determining their potential as anti-breast cancer drugs.

Almeer, R., *et.al*. [133] noticed interaction green platinum nanoparticles synthesized by using leaf extract of *Azadirachta indica* with HEK293 cells. Green platinum nanoparticles induced oxidative stress and reducing the level of GSH lead to damage of the components of HEK293 cells. Green platinum nanoparticles compromise apoptosis by mitochondrial and caspase-3- dependent manner in HEK293 cells.

Gurunathan, S., *et. al*. [134] studied the toxicological properties of PtNPs, synthesized ultra-small by using Apigenin on cytotoxicity, genotoxicity, and proinflammatory responses in the human monocytic cell line (THP-1). Monitoring obviously indicated that PtNPs induce cytotoxicity in a dose-dependent manner by decreased cell viability and proliferation.

Al-Radadi, N., *et.al*. [135] studied green synthesis of the platinum nanoparticle via the dates of Ajwa and Barni extract that worked as capping and a reducing agent. The size of the obtained PtNPs was small and spheric homogenous shapes. PtNPs were achieved with Ajwa and Barni extract effect on hepatocellular carcinoma cells (HepG-2), colon cancer HCT, and breast cancer cells (MCF-7). The PtNPs obtained used to

inhibit the growth of Gram-negative bacteria *Escherichia coli* and Gram-positive bacteria *Bacillus subtilis*.

Aygun, A., *et.al*. [136] studied the biogenic platinum nanoparticles (PtNPs) that synthesized by using black cumin seed (Nigella sativa L.) extract as a reducing factor. Pt nanoparticles have spherical shapes and small sizes. the biogenic PtNPs were estimated for their cytotoxicity influence on MDA-MB-231 breast and HeLa cervical cancer lines and their anti-bacterial impact against selected strains of Gram-positive and Gram-negative bacteria. The cytotoxicity and bacterial screening showed the effectiveness of biogenic Pt nanoparticles.

Selvi, A., *et.al*. [137] studied possibility pharmaceutical platinum nanoparticles synthesized by means of leaf extract of *Tragia involucrata* for overall therapeutic purposes. That showed excellent anti-oxidant, anti-bacterial, and anti-cancer activity mitochondria-associated apoptosis in HeLa cells, which is very hopeful for pharmaceutical applications.

Gurunathan, S., *et.al*. [138] "Anti-cancer Properties of Platinum Nanoparticles and Retinoic Acid: Combination Therapy for the Treatment of Human Neuroblastoma Cancer." used an approach to synthesize PtNPs using beta carotene as templates, these findings propose that PtNPs and Retinoic acid acted synergistically to induce apoptosis and may have the possibility for combination biotherapy in the treatment of malignant diseases such as neuroblastoma.

1.26 Aim of the current study

The main objective of this research:

1. Synthesise platinum nanoparticles by utilizing biological methods as an alternative strategy to the traditional synthesis of nanoparticles.
2. Study the characters of prepared platinum nanoparticles by UV-Visible, FT-IR, XRD, TEM, AFM, and SEM.
3. Determine the cytotoxicity of prepared platinum nanoparticles on the Ovarian cancer SKO-3 and Oesophageal cancer SK-GT-4 cell lines using MTT assay.
4. Evaluate the antibacterial action of prepared platinum nanoparticles against Gram-negative bacterial strain *pseudomonas aeruginosa* and Gram-positive bacterial strain *Streptococcus pyogenes*. by using the agar well diffusion technique.

CHAPTER TWO

2. Experimental part

2.1 Chemical materials

All chemicals used in this study are shown in Table (2-1) .

Table (2-1) List of chemicals used in this study

No.	Materials	Formula	M.WT	Supplier From	Manuf. Country	Purity%
1	Hydrated hexachloroplatinic	$H_2PtCl_6.6(H_2O)$	517.91 g/moL	Sigma-Aldrich	USA	99.9%
2	Deionized water	H_2O	18 g/moL	Chem-Lab	Belgium	100%
3	Trypsin/EDTA	———	———	Capricorn	Germany	——
4	DMSO	C_2H_6OS	78.13 g/moL	Santacruz Biotech	USA	99%
5	RPMI 1640	———	———	Capricorn	Germany	——
6	MTT stain	$C_{18}H_{16}BrN_5S$	414.32 g/moL	Bio-World	USA	95%
7	Fetal bovine serum	———	———	Capricorn	Germany	——
8	Muller hinton agar	———		Hi-Media	India	——

2.2 Instruments and apparatus

All chemicals used in this study are shown in Table (2-2).

Table (2-2): List of instruments and apparatus are used in research

No.	Instruments	Manufacturing Company	Source
1	Analytical balance	Mettler Toledo	Switzerland
2	Hot plate stirrer	Alfa (HS-860)	Iran
3	Centrifuge	Mindray	China
4	Scanning electron Microscope	ZEISS GeminiSEM	Germany
5	Transmission electron microscope	ZEISS	Germany
6	Atomic force microscope	ZEISS Integrated	Germany
7	X-ray Diffraction	philips PW1730	Dutch
8	Fourier-transform infrared spectrophotometer	IRAffinity-1- Shimadzu	Japan
9	UV-Visible spectrophotometer	Shimadzu UV-160 A	Japan
10	CO_2 incubator	Cypress diagnostics	Belgium
11	Microtiter reader	Gennex lab	USA
12	Laminar flow hood	K & K scientific supplier	Korea
13	Micropipette	Cypress diagnostics	Belgium
14	Cell culture plates	Santa cruz biotechnology	USA

2.3 Stock solution of [$H_2PtCl_6.6(H_2O)$]

0.01M stock solution of hydrated hexachloroplatinic [$H_2PtCl_6.6(H_2O)$] was done by dissolving 0.517g of dried hydrated hexachloroplatinic [$H_2PtCl_6.6(H_2O)$] in 100 mL deionized water.

2.4 Prepare dates

Two types of well-known Iraqi dates were used, namely, Al-Khastawi and Al-Zahidi dates; after collection, they were cleaned of impurities, washed with deionized water, and dried by hot air in the oven at a temperature of 90°C as shown in Figure (2-1) .

Figure (2-1): Prepare of dates

2.5 Preparation of dates extract

To prepare the dates extract, 50.5 g of Al-Zahidi dates and 47.45 g of Al-Khastawi dates were weighed, 250 mL of deionized water was added as a solvent. The amount was decreased to 150 mL after boiling at a temperature of 100°C for 25 minutes. The solution was filtered using Whatman filter paper No. 1 to produce the filtrate (extract), which was kept in a hot and dark position and used within a day as shown in Figure (2-2) .

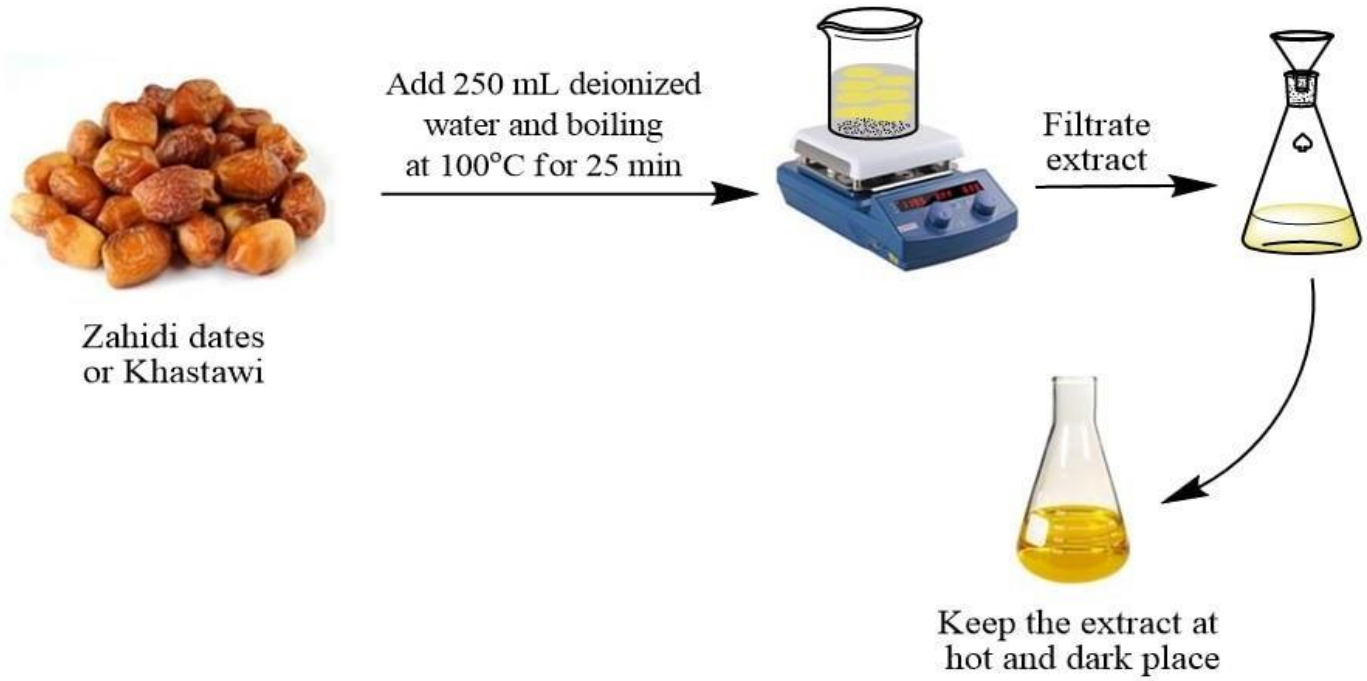


Figure (2-2): Preparation of dates extract

2.6 Green syntheses of platinum nanoparticles

To prepare platinum nanoparticles in this experiment, (2,4,6,8 and10) mL of each of Zahidi and Khastawi dates extract were taken as shown in Figure (2-3).

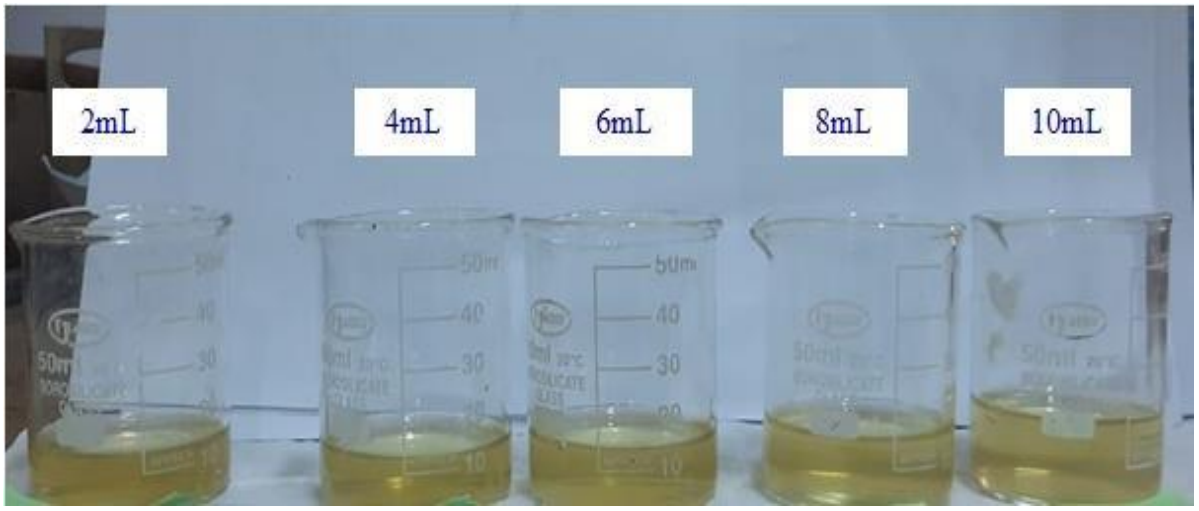


Figure (2-3): Exhibit volumes were taken for each Zahidi and Khastawi dates extract.

Dates extracts were mixed with 5mL of stock solution of $[H_2PtCl_6.6(H_2O)]$ with heating for 20 minutes at a temperature 90°C . Deionized water was added to complete the volume to 20 mL and then the solution pH was adjusted to 8.5 using 0.1M NaOH as shown in Figures (2-4). Based on variables such as temperature, pH, concentration, and time, the solutions changed their color from yellow to brown or yellowish-brown as shown in Figures (2-5).

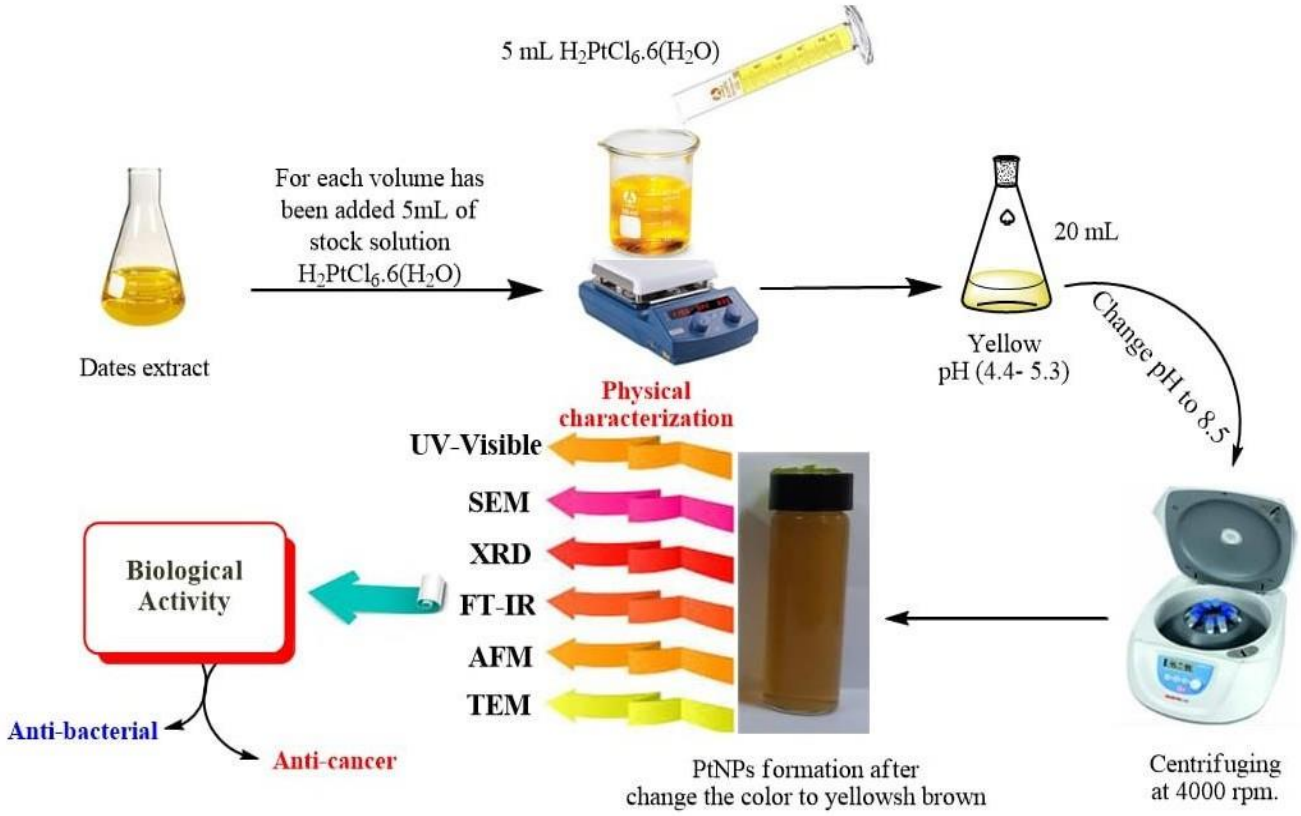
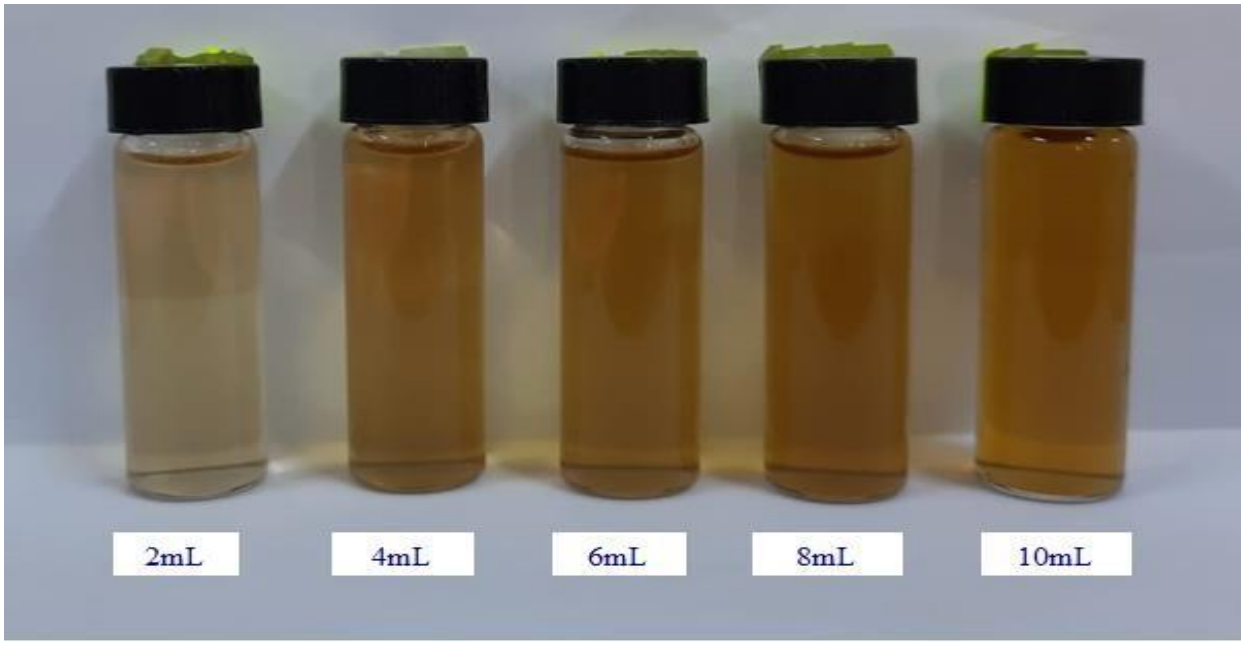


Figure (2-4): Illustration graphic for green synthesis of platinum nanoparticles from Zahidi or Khastawi dates extract



Figures (2-5): Exhibit solutions after changed their color from yellow to brown or yellowish-brown

2.7 Characterization of Pt nanoparticles

The purpose of the measurement methods is to define the properties, composition, and structure of the prepared nanoparticles. Characterization of nanoparticles can be assorted into two essential groups namely; quantitative and qualitative. These methods involve a range of different developed techniques like, UV–Vis spectroscopy, fourier transform infrared spectroscopy, X-ray diffraction, scanning electron microscopy, transmission electron microscopy, and atomic force microscopy, characteristics can be studied using some of these techniques which are helpful to determine diverse parameters such as particle size, shape, crystallinity, fractal dimensions, pores size, and surface area [(139)].

2.7.1 UV-Visible spectroscopy

The absorption spectrum of the nanoparticles solution was measured by, Shimadzu; Device model: UV-160 A at the University of Tehran-Iran. The measurements were done at room temperature 27 °C in the quartz cell. To suspend the materials, deionized water was used .The samples were measured between (200 -800) nm.

2.7.2 Fourier transform infrared spectroscopy (FT-IR)

The functional groups included in the examined nanoparticles were identified using a Fourier transform infrared instrument at wavelength ranging from (400 – 4000) cm^{-1}. Prepared nanoparticles were examined by IRAffinity-1- Shimadzu ; at BPC Analysis center in Baghdad. All measurements were carried out at room temperature 27 °C.

2.7.3 X-ray diffraction (XRD)

X-ray diffraction for prepared nanoparticles was examined by XRD device model philips PW1730 ; at the University of Tehran-Iran. The technique of X-ray diffraction was used to investigate the crystalline structure of materials since the X-ray wavelengths between (0.2 and 10) nm are comparable to the interatomic spacing of crystalline solids. The method determines the average distance between atoms in layers or rows. The XRD technique enables one to evaluate the direction of a single crystal or grain and the scale and form of small crystalline regions as shown in Figure (2-3).

The diffraction of X-rays by a crystal is explained by the Bragg law, which is defined as the relationship between the wavelength of the X-rays and the interatomic spacing and is given by the following equation [(140)]:

$$\lambda = 2d \sin\theta \quad \ldots\ldots\ldots (1)$$

where λ is the wavelength of the X-ray, d is the interlayer spacing, and θ is the incident angle as shown in Figure (2-6) [(141)]. Apparent

crystallite sizes are obtained from the Debye Scherrer equation to determine various characteristics of the crystalline material

$$D = 0.9\lambda/\beta \cos\theta \ldots\ldots (2)$$

where **D** is the crystal size, **λ** is the wavelength of X-ray, **θ** is the Braggs angle in radians, and **β** is the full width at half maximum of the peak in radians [142].

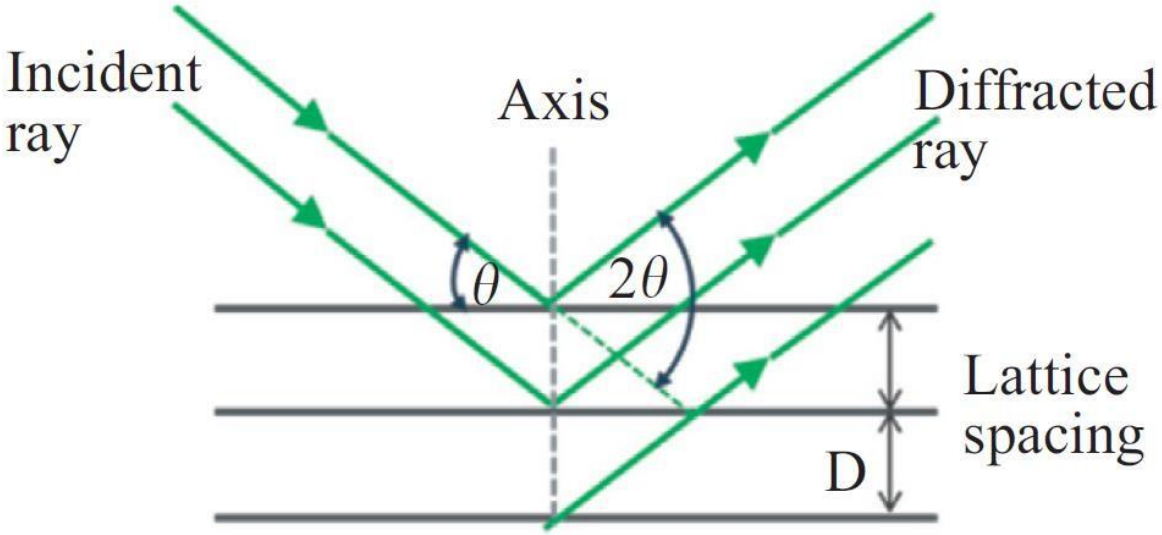


Figure (2-6): X-ray diffraction [141].

2.7.4 Transmission electron microscope(TEM)

Transmission electron microscope is a form of microscopy in which a ray of electrons is passed across a very thin specimen, interfering with it as it travels. The interaction of electrons transferred through the specimen produces an image, which is magnified and focused onto an imaging device, such as a fluorescent screen, a sheet of photographic film, or to be discovered by a sensor [143] as shown in Figure (2-7). The device used is the Germany origin Zeiss was used at the laboratories of University of Tehran – Iran.

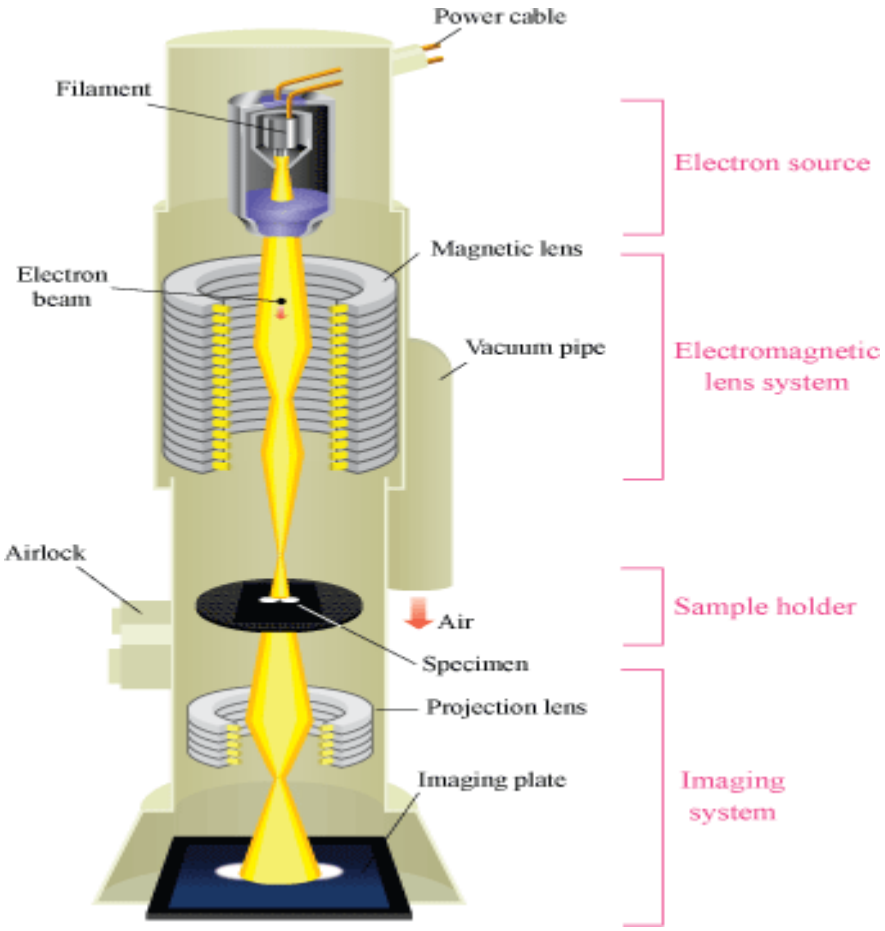


Figure (2-7): Schematic diagram of TEM system.

2.7.5 Scanning electron microscope (SEM)

SEM is a surface imaging technique in which an incident electron beam scans over the specimen surface and interacts with it, generating signals that represent the specimen atomic composition and topographic information. SEM generates images with much better resolution by using accelerated electron beams and electrostatic or electromagnetic lenses [144] as shown in Figure (2-8). Scanning electron microscope was utilized to assay nanoparticles samples at University of Tehran-Iran .

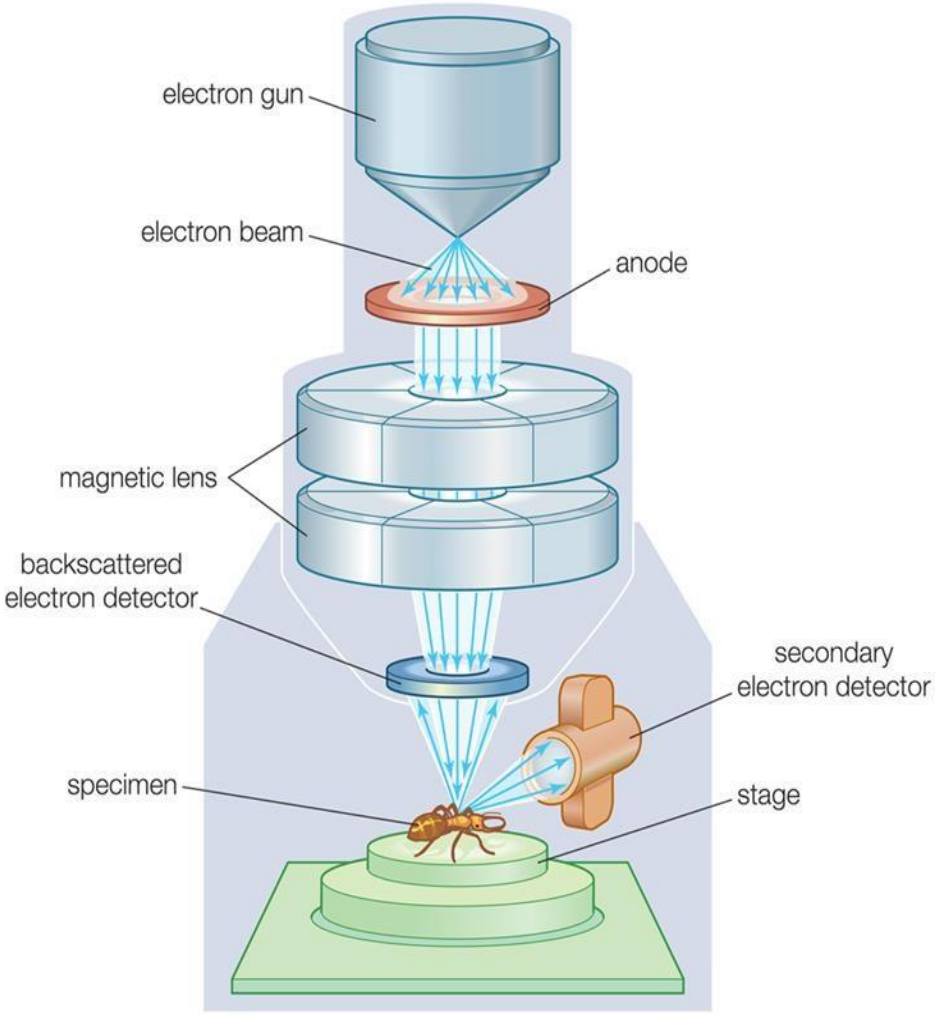


Figure (2-8): Scanning electron microscope

2.7.6 Atomic force microscope (AFM)

Atomic force microscopy was used to scan the surface of nanomaterials with the use of a probe as shown in Figure (2-9), which creates very high-resolution images. Atomic force microscopy, was used to physically scan material at the submicron level that resulting in high-resolution photographs of the particle size measurement. The AFM method was used to investigate the size, shape, structure, dispersion, and aggregation of nanomaterials [145].

ZEISS integrated atomic force microscope was used at the University of Tehran- Iran.

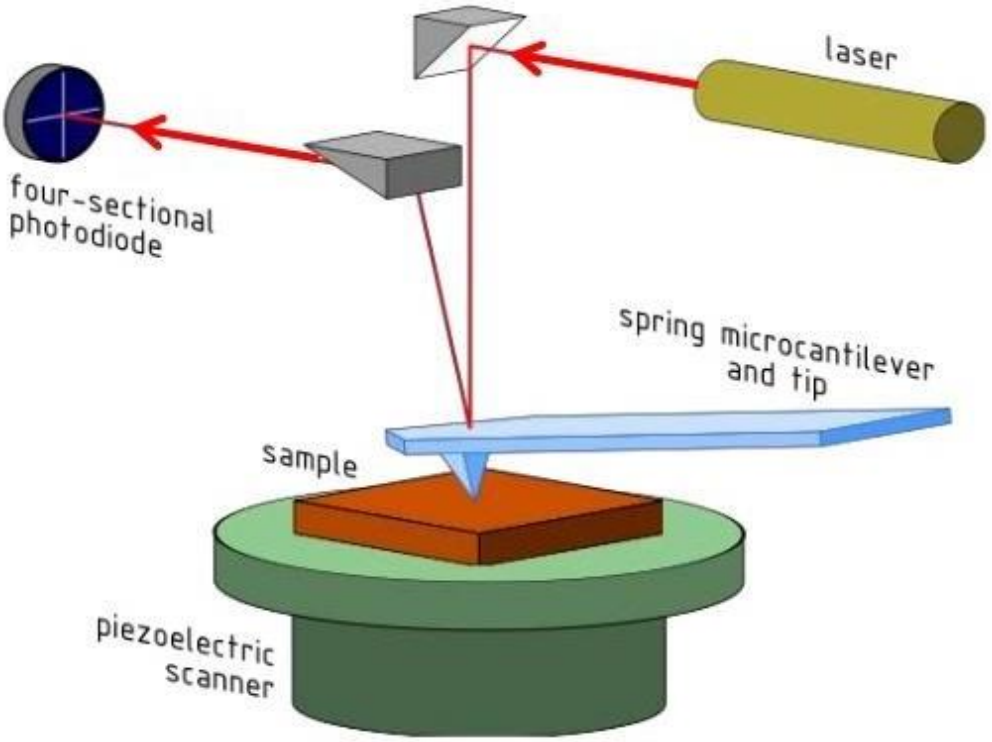


Figure (2-9): Schematic diagram of AFM

2.8 Biological applications of prepared platinum nanoparticles

2.8.1 Anti-cancer activity of prepared PtNPs

2.8.1.1 Cell cultures

SKO-3 and SK-GT-4 cells were maintained in RPMI-1640 supplemented with 10% foetal bovine serum, 100 units/mL of penicillin, and 100 µg/mL of streptomycin. The cells were then passaged using Trypsin-EDTA reseeded at 80% confluence twice a week and incubated at 37 °C [146,147].

2.8.1.2 Determine cytotoxicity using MTT assay

The MTT assay was conducted using 96-well plates to determine the cytotoxic effect of PtNPs [148,149]. Cell lines were seeded at 1×10^4 cells/well. Cells were treated with tested compounds at different concentrations after 24 hours or a confluent monolayer was achieved. Cells viability were measured after 72 hours of treatment by removing the medium, adding 28 µL of 2 mg/mL solution of MTT, and incubating the cells for 2.5 hours at 37 °C. The remaining crystals in the wells after removing the MTT solution are solubilized by the addition of 130 µL of DMSO followed by 37 °C incubated for 15 min with shaking [150]. The absorbency was determined on a microplate reader at 492 nm and the assay was performed in triplicate. The inhibition rate of cell growth (the percentage of cytotoxicity) was calculated as follows [151,152]:

Inhibition rate = A- B/A*100.....(3)

A is the optical density of control and **B** is the optical density of the samples [138]. The cells were seeded into 24-well microtitration plates at a density of 1×10^5 cells mL^{-1} and incubated for 24 h at 37 °C to visualize the shape of the cells under an inverted microscope. The cells were then exposed to PtNPs at IC50 concentration for 24 hours. Afterward, the plates were stained with crystal violet stain and incubated at 37 °C for 10–15 min after the exposure time [153]. The stain was washed off gently with tap water until the dye was completely removed. The cells were finally observed under an inverted microscope at 100x magnification, and the images were captured with a digital camera attached to the microscope [154,155].

2.8.2 Anti-bacterial activity of prepared PtNPs

2.8.2.1 Determine inhibition of prepared PtNPs

The anti-bacterial behaviour of the prepared PtNPs was examined against Gram-negative bacterial strain *P. aeruginosa* and Gram-positive bacterial strain *S. pyogenes* via agar-well diffusion technique [156]. Approximately 20 mL of Muller–Hinton (M–H) was aseptically poured into sterile Petri dishes before cultivation [146]. The bacterial species were obtained from their stock cultivars using a sterile wire loop. After the cultivation of species on the agar plates, 6 mm diameter wells were drilled using a sterile tip [157]. Various amounts of bare PtNPs (0.01, 0.005, 0.00250, 0.00125) M were used in the agar wells. Cultivated PtNPs containing plates and test organisms were then incubated overnight at 37 °C before measuring and recording the average diameter of the bacterial inhibition zones formed by the respective PtNPs concentrations. The experiments were conducted in triplicate [158].

2.9 Statistical analysis:

The obtained data were statically analyzed using an unpaired *t-test* with Graph Pad Prism 6 [159]. The values were presented as the mean ± SD of triplicate measurements [160].

CHAPTER THREE

3. Results and discussion

3.1 Synthesis of platinum nanoparticles (PtNPs)

The method of the production of nanoparticles starts by combining a metal–salt solution with a sample of plant extract. The biochemical reduction of the salt solution occurs , and the reaction mixture changes color, signaling the existence of nanoparticles [161]. In this study, platinum nanoparticles were synthesized by the reduction of $Pt^{+\ 4}$ to Pt^{0} that is generated by the addition of hydrated hexachloroplatinic [$H_2PtCl_6.6(H_2O)$] solution to the dates extract .The extract contained phytochemicals compounds that could work as reducing and capping agents .The color of the solution changed from yellow to brown or yellowish-brown, indicating the formation of PtNPs.

3.2 PtNPs formation mechanism

In plant based sources the bioactive compounds e.g. polyphenols has the dual role of a reductant and a capping agent for preserving the stabilization of metal nanoparticles [162]. The functional groups present in the zahidi and khastawi dates extract compound is thought to be the source of reducing and surface capping agents stabilizing the PtNPs. The hydroxyl functional groups in the polyphenols reduce Pt ions to PtNPs and cap to form stabilized PtNPs., The foundations of synthesis can be demonstrated in two stages: Pt atoms (Pt^{0}) are formed in the first step as a result of the reduction of various complexes with Pt^{4+} ions, followed by the forming of oligomeric clusters as a result of agglomeration, and these clusters ultimately contribute to the formation of colloidal PtNPs in the second step. The bio-reduction pathway is heavily influenced by functional groups such as amine (-NH), alcohol (-OH), carboxylic group (-COO), and amide. Groups, such as hydroxyl, are oxidized during the reduction and

stabilization process, resulting in oxidized forms that start capping the surface of the PtNPs. As a result, the functional groups in the zahidi and khastawi dates extract compounds may be responsible for the bio-reduction of Pt^{+4} ions to metallic PtNPs as shown in Figure (3-1) [163].

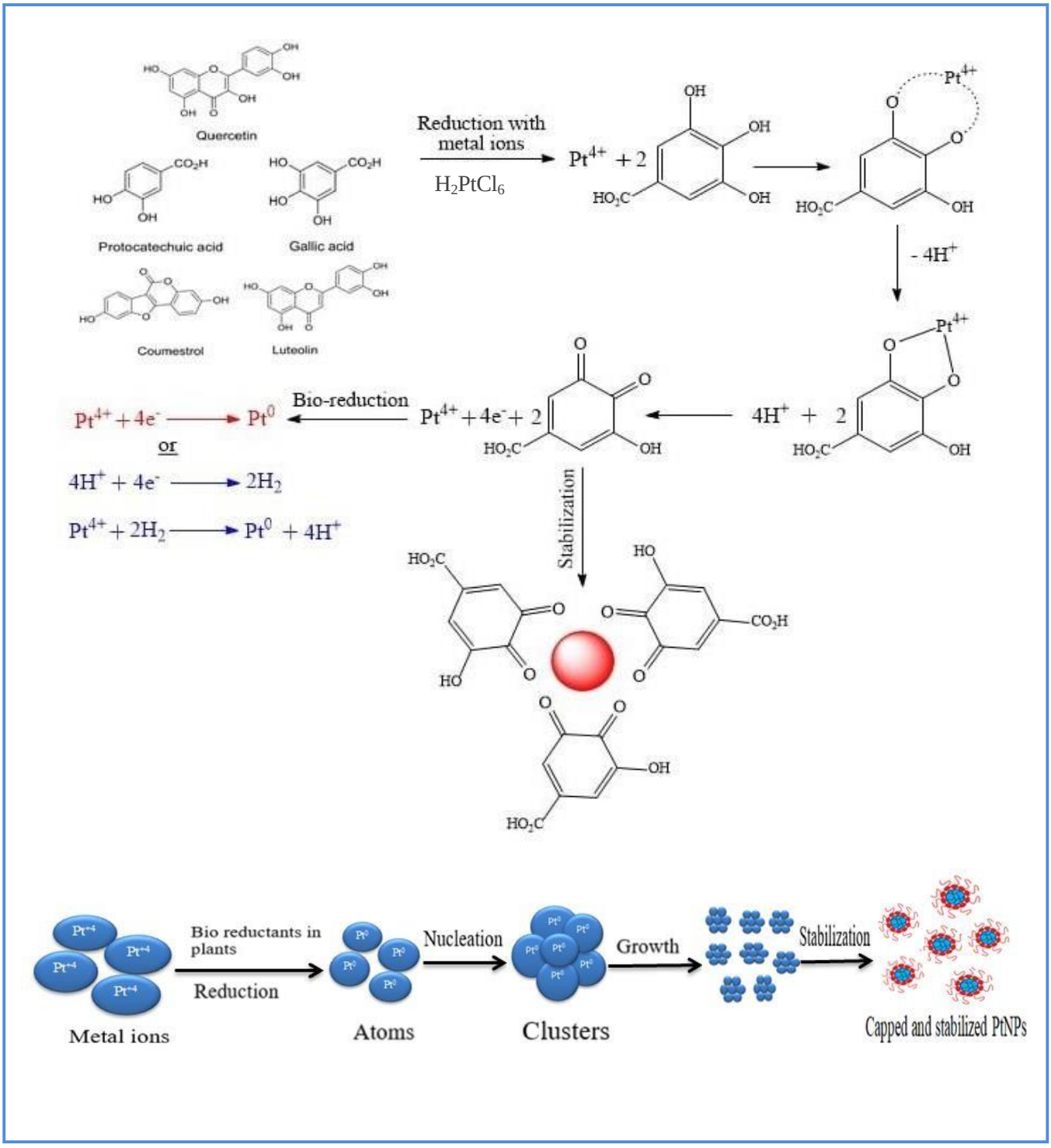


Figure (3-1): Proposed mechanism for biofabrication and stabilization of PtNPs by extract of plants.

3.3 Identification of prepared platinum nanoparticles

3.3.1 Measurement of UV-Visible spectroscopy

UV–Vis spectroscopy is an absorption spectroscopy technique used to validate nanoparticle synthesis. It was used to as-certain the existence of synthesized platinum nanoparticles in this study. The UV-Visible spectrum of platinum nanoparticles synthesized using extracts of zahidi and khastawi dates are presented in Figure (3-2). The UV-Visible spectra showed surface plasmon resonance (SPR) bands around 283 nm for PtNPs, Surface plasmons are charge density oscillations of free electrons in a metal that cause surface plasmon waves to be generated, an absorbance peak signaled the formation of platinum nanoparticles was detected [(164)]. The solutions' color change from yellow to yellowish-brown could be used to track the production of platinum nanoparticles. This marked the formation of platinum nanoparticles as a result of the reduction process of Pt^{4+} to Pt^{0} nanoparticles.

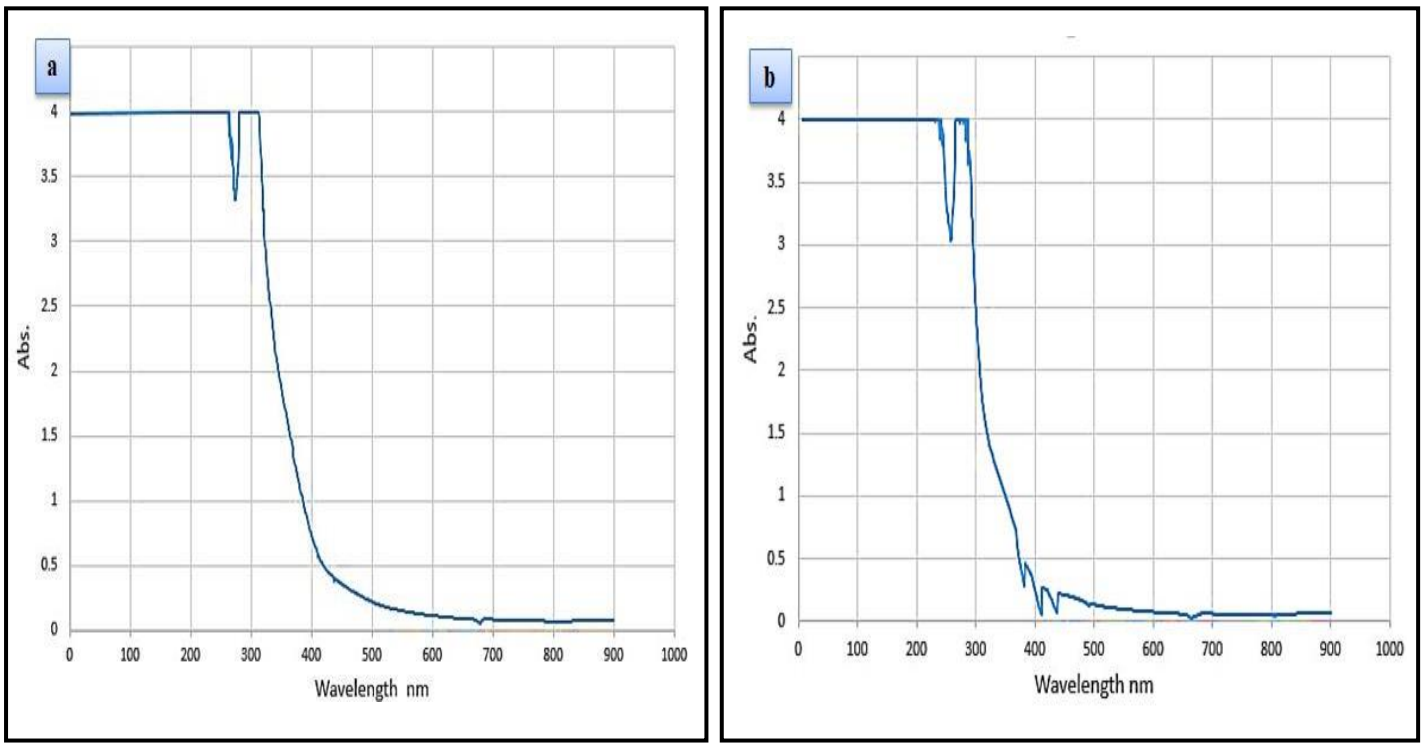


Figure (3-2): UV–Vis absorption spectrum of green synthesized platinum nanoparticles using (a) Zahidi and (b) Khastawi dates extract.

3.3.2 Fourier transforms infrared spectroscopy analysis

FT-IR spectroscopic analysis was applied to observe the possible biomolecules present in zahidi dates extract as shown in Figure (3-3a), such as proteins and flavonoids. These biomolecules work as a reducing source and stabilising agent to PtNPs synthesized by zahidi dates extract. FT-IR spectra of PtNPs in Figure (3-3b) demonstrates peaks at (3302.13, 1639.49, 1234.44 and 1026.13) cm^{-1}. The broad peak at 3302.13 cm^{-1} is associated with –OH stretching vibration of phenolic compounds, whilst that at 1639.49 cm^{-1} is associated with C=O stretching vibrations. The two peaks at (1234.44 and 1026) cm^{-1} are associated with the stretching vibration of C−O and C−N stretching.

The FT-IR spectrum of synthesized PtNPs illustrated a decrease in the peak intensities of the functional groups compared with the functional groups in dates extract. The absence of these functional groups in the synthesized PtNPs indicates the formation of PtNPs. Identified sharp peaks in the range of (420.48–532.35) cm^{-1} refer to the vibration of PtNPs. This result means that PtNPs were formed successfully [165,166].

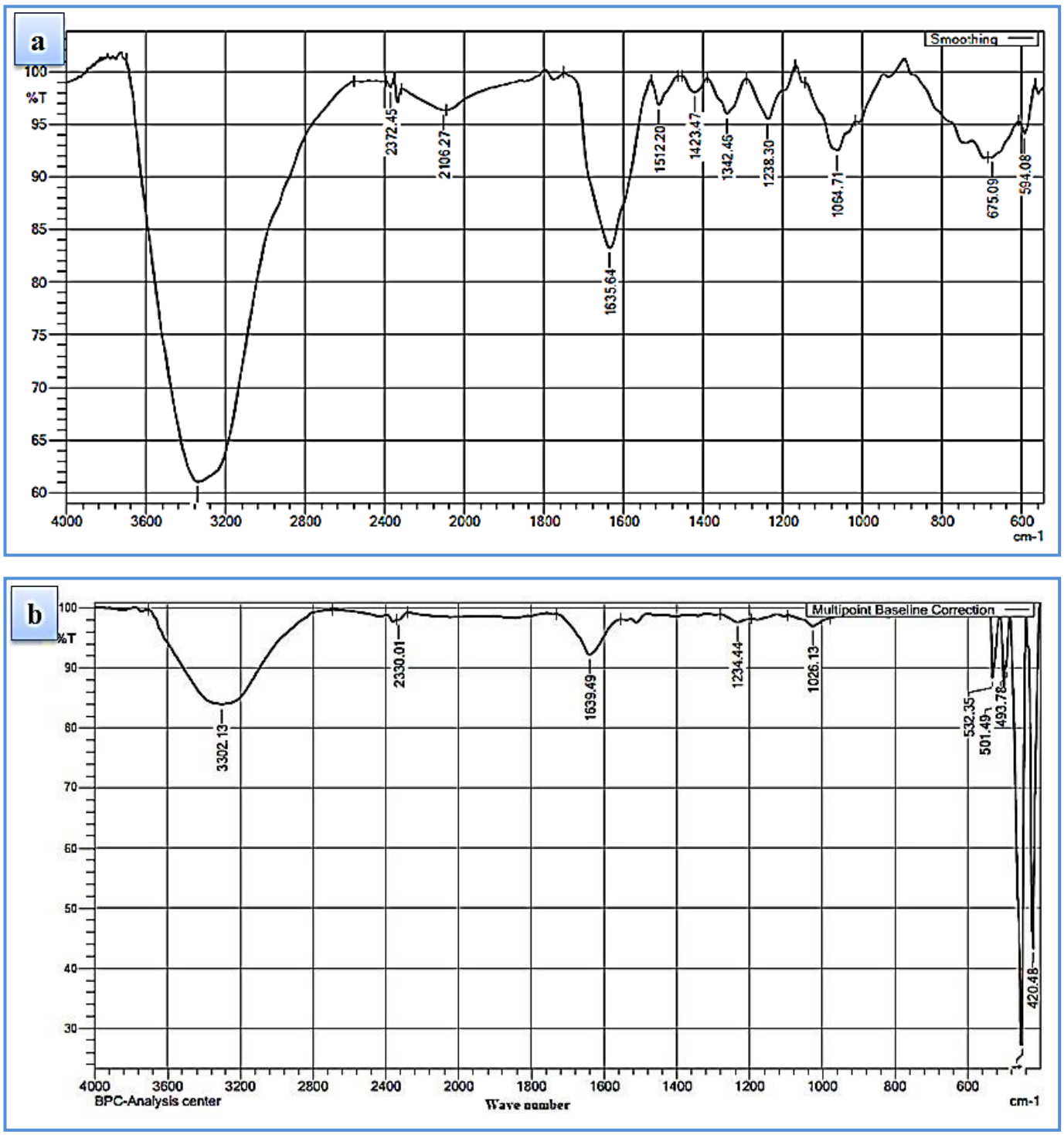


Figure (3-3): FT-IR spectrum of (a) zahidi dates extract and (b) The prepared PtNPs

Figure (3-4a) and Figure (3-4b) show the FT-IR spectra of the khastawi dates extract and PtNPs prepared were conducted to determine the functional groups of biosynthesized platinum nanoparticles . The FT-IR bands spotted at (3325.28, 1770.65, and 1600) cm^{-1} in khastawi dates extract attributed to the O–H, C=O, and C–N respectively. The stretching bands for the O–H and C=O groups that may interact with PtNPs can be found in amino acids.

The strong band at 1249.87 cm^{-1} can be appropriate to the C–O and its shift in vibration to 1238.30 cm^{-1} for PtNPs . Also, the disappearing of the strong band at 1770.65cm^{-1} in PtNPs indicating that polyphenols of khastawi dates extract are responsible for the bio-reduction and capping of the PtNPs. The disappearance of N–H stretching frequency (2931.80 and 2873.94) cm^{-1} indicates abounding of the biomolecules to the Pt nanoparticles through the N–H group of amino acids. Also, the band at 1600 cm^{-1} in the khastawi dates extract appointed as C–N vibrations almost disappeared, indicating the participation of protein amide in the bounding to the Pt nanoparticles [167,168].

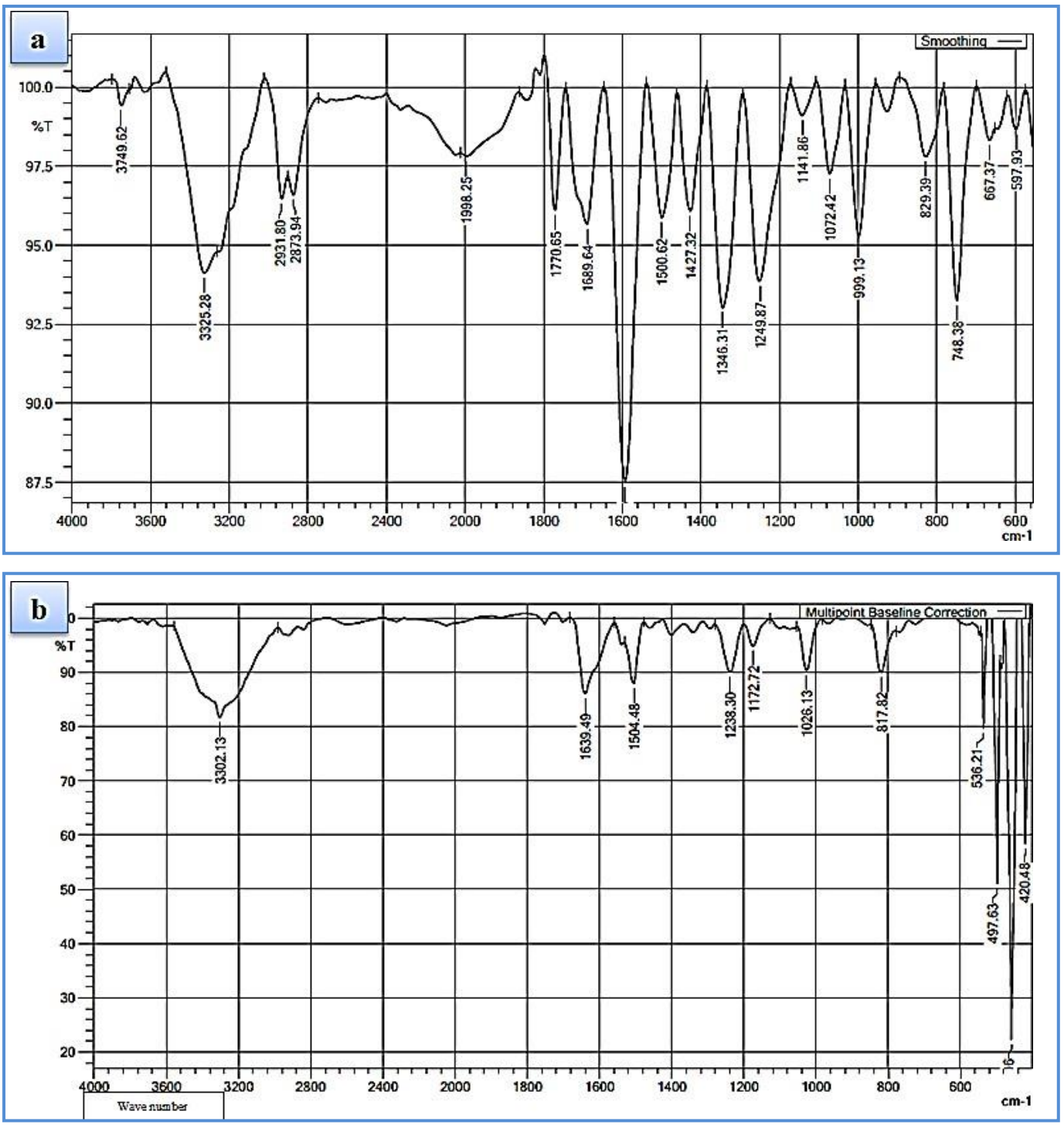


Figure (3-4): FT-IR spectrum of (a) Khastawi dates extract and (b) the prepared PtNPs

3.3.3 X-ray diffraction analysis (XRD)

PtNPs synthesized using zahidi dates extract and khastawi dates extract are crystalline . PtNPs reveal a face-centered cubic structure. The XRD spectra comparative to the standard confirmed that spectrum of platinum particles produced in the experiments were in the shape of nanocrystals. As demonstrated by the peaks at 2θ values of the 38.48°, 44.77°, 65.20°, and 77.95°, which were respectively assigned correspond to diffraction peaks of (111), (200), (220), and (311), as shown in Figures (3-5) and (3-6) [169].

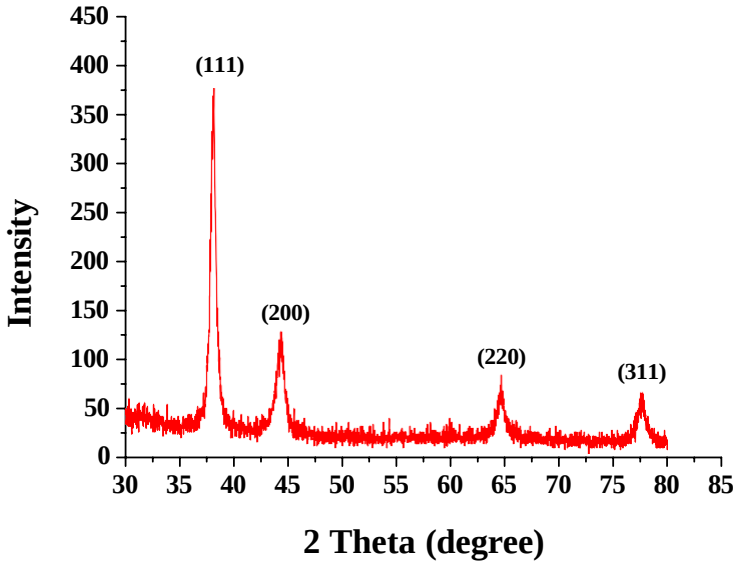


Figure (3-5): XRD of PtNPs synthesized by zahidi dates extract.

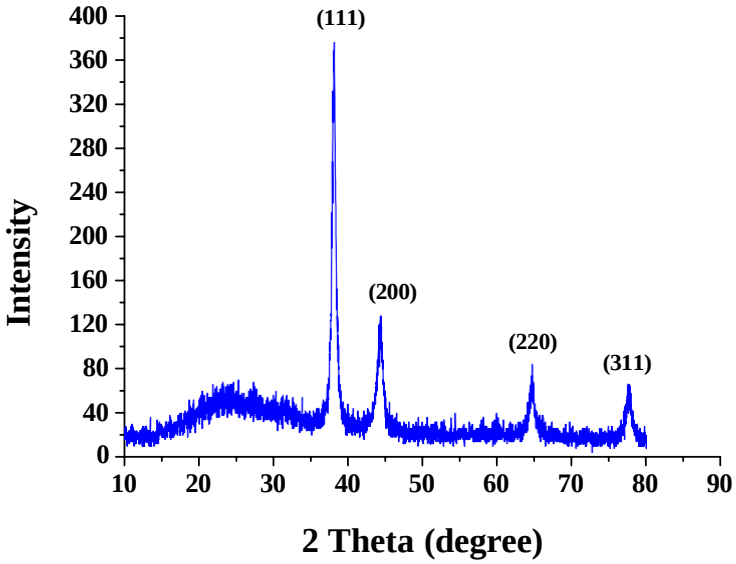


Figure (3-6): XRD of PtNPs synthesized by Khastawi dates extract.

Average crystal size in the product that can be found using X-ray diffraction profile. Calculating the crystal size (D) can be done by using the Debye Scherrer equation [170]:

D = $K\lambda\beta COS\theta$.....(2)

The average particle size of the fabricated PtNPs was determined using the Debye–Scherrer equation, which expounds the relationship between crystallite size peak broadening in XRD. in which D is the mean diameter of nanoparticles, K is the Scherrer constant with a value of 0.9, λ is the wavelength of the X-ray radiation source 0.15406 nm, and θ is the Bragg's angle [162].

Table (3-1): Structural parameter of PtNPs

No.	Pos. [°2Th.]	FWHM Left [°2Th.]	d-spacing	Height [cts]	Rel. Int. [%]	Crystallite Size [Å]	Crystallite Size [nm]	Micro Strain only [%]
1	38.4648	0.1036	2.33849	123.44	100	820.444	82.0444	0.089225
2	44.4293	0.1145	2.03741	58.43	47.34	932.165	93.2165	0.109284
3	65.1921	0.09	1.42989	17.47	14.16	1266.63	126.663	0.021886
4	77.83(3)	0.036	1.22633	57(512)	46.26	1589.54	158.954	0.001709

3.3.4 Transmission electron microscope analysis

TEM analysis was recorded to study the morphological characterization and determine the size and structure of PtNPs. The images show that most PtNPs have spherical shapes as shown in Figure (3-6). The nanoparticles are arranged roughly parallel to each other, with a significant amount of small-size nanoparticles. In addition, the synthesised PtNPs are formed in large quantities. The PtNPs were exhibited in diameter ranging from (30 – 40) nm, which is compatible with the X-ray result.

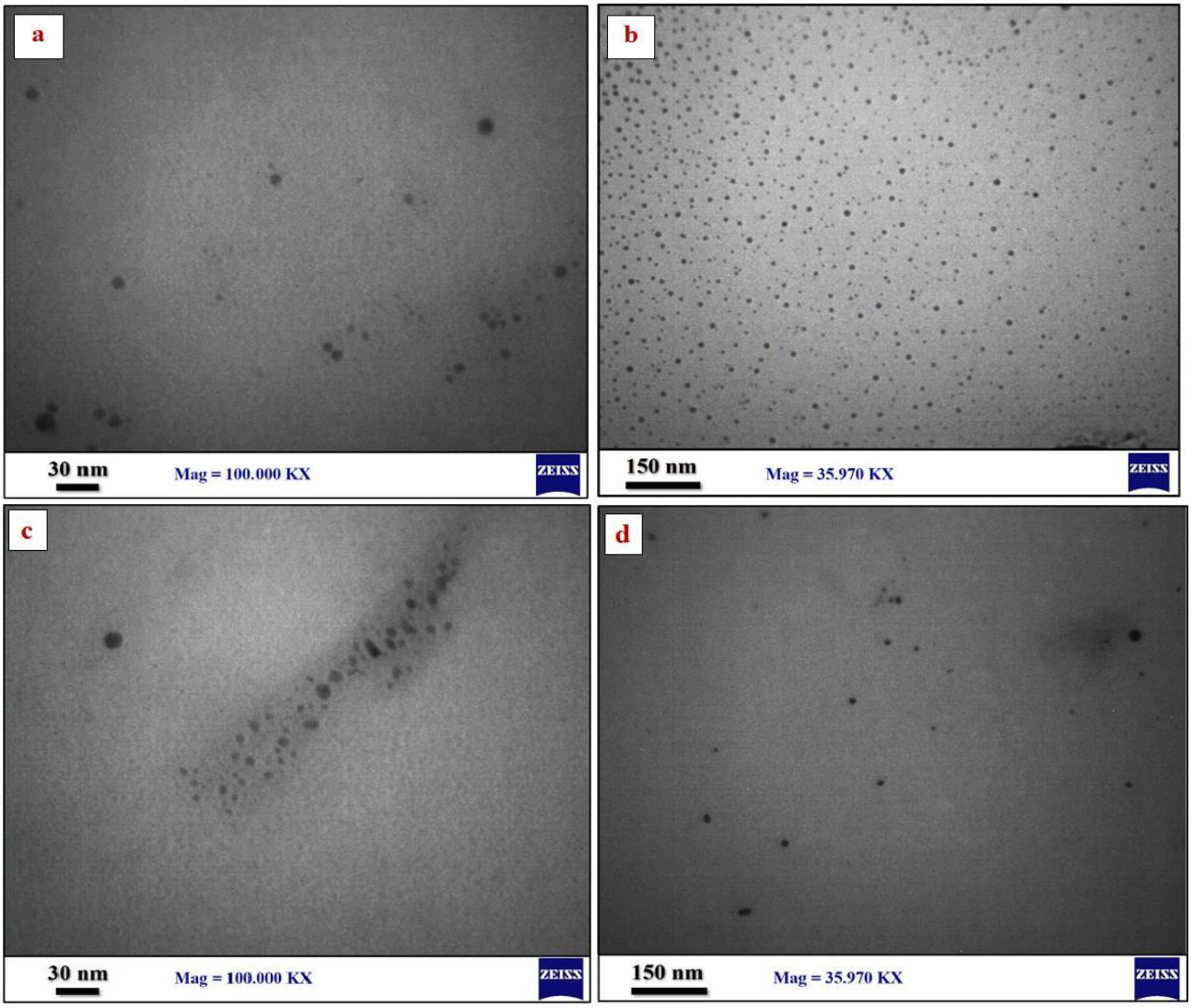


Figure (3-7): TEM micrograph PtNPs of zahidi extract (a) 30 nm (b) 150 nm and khastawi extract (c) 30 nm, (d) 150 nm.

3.3.5 Scanning electron microscope analysis

SEM analysis was accomplished to determine the shape and surface morphology of PtNPs prepared from aqueous zahidi and khastawi dates extracts with diameters ranging from 30 nm to 40 nm, as demonstrated in the SEM images presented in Figure (3-7).

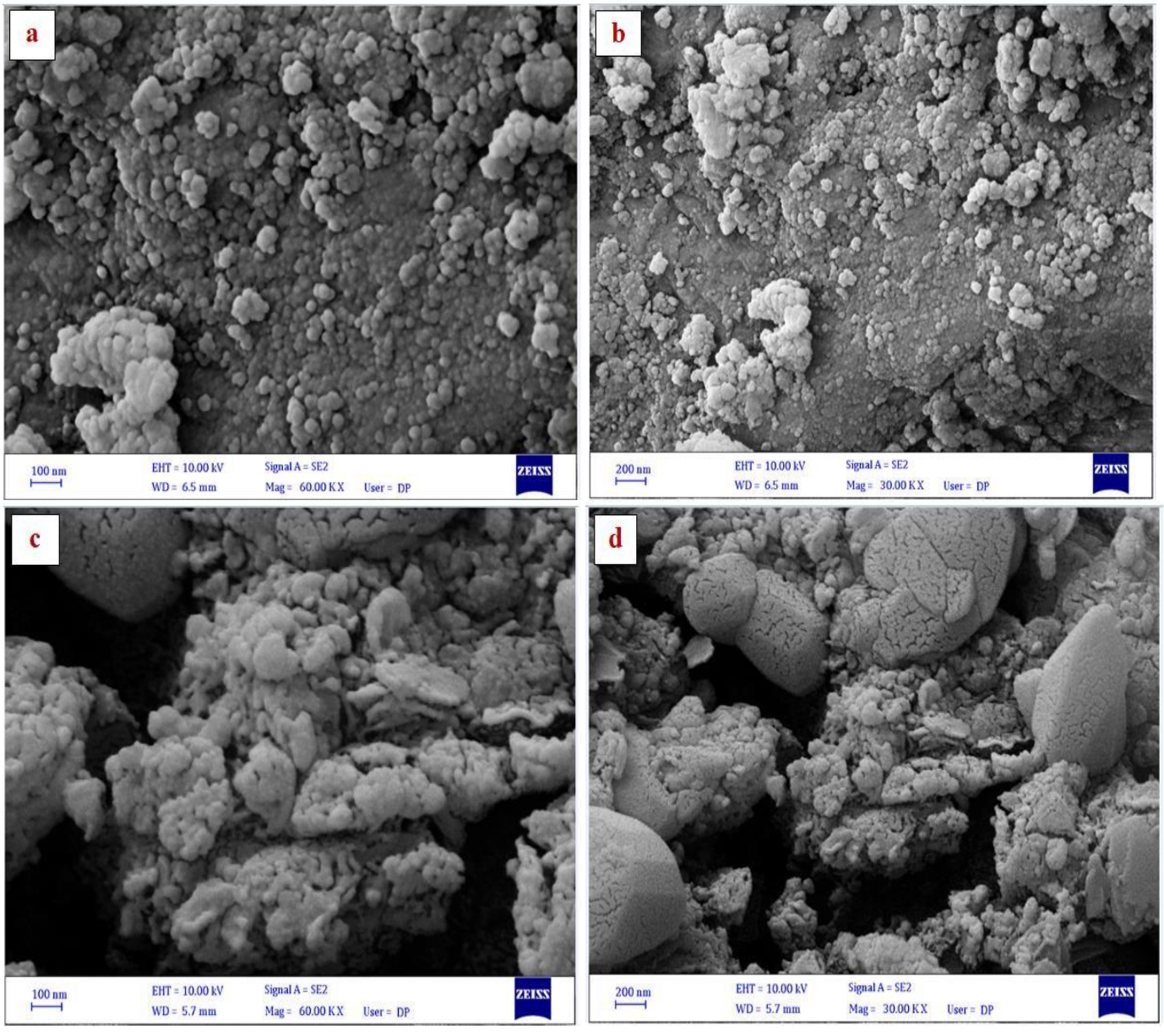
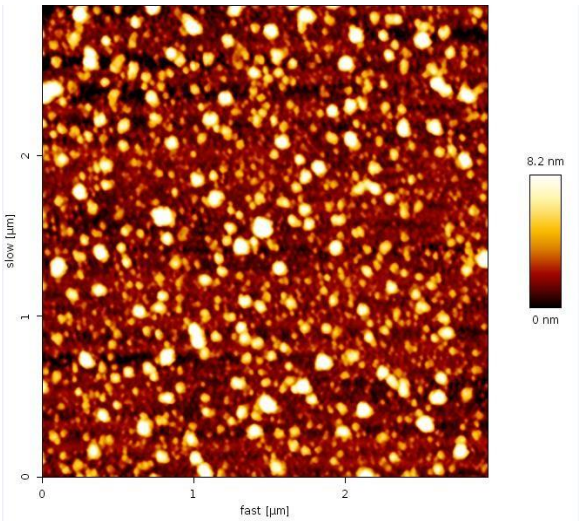
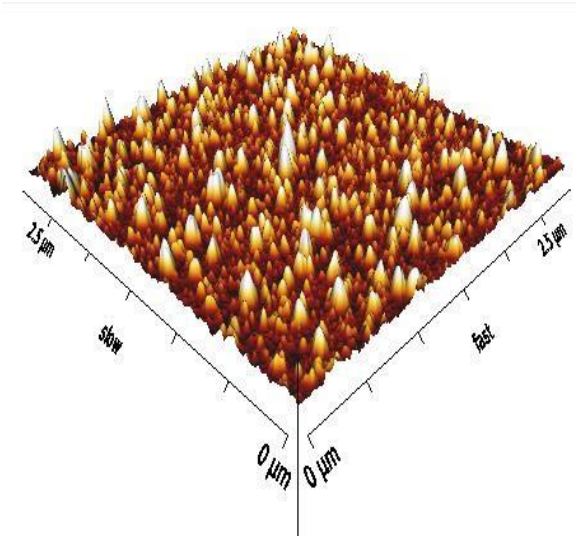


Figure (3-8): SEM micrograph of synthesis PtNPs by zahidi extract (a) 100 nm (b) 200 nm and khastawi extract (c) 100 nm (d) 200 nm.

3.3.6 Atomic force microscope analysis (AFM)

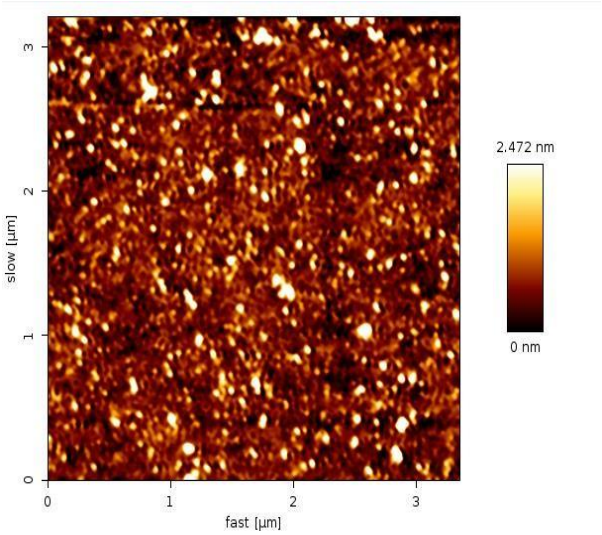
The characterisation of PtNPs was also checked via AFM, as shown in Figure (3-8). The Figure displays the two- and three-dimensional images of synthesised PtNPs. The images revealed that the distribution of PtNPs with a diameter of (30–40) nm was limited.

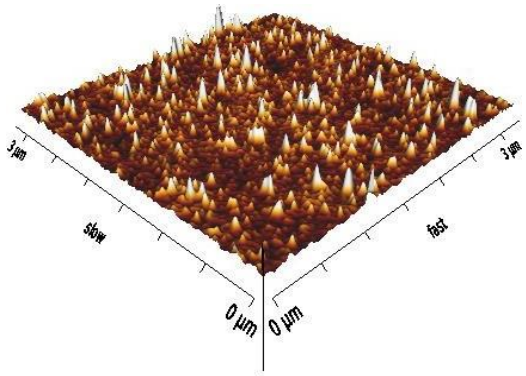




3.3.6.1

(b)





(c)

(d)

Figure (3-9): AFM analysis of PtNPs by zahidi extract (a) 2-dimension and, (b) 3-dimension structure and khastawi extract (c) 2-dimension and (d) 3-dimension structure.

3.4 Biological applications of prepared platinum nanoparticles

3.4.1 Anti-cancer activity of prepared PtNPs

Many cancer chemotherapeutic drugs available for treating work to destroy malignant tumor cells by inhibiting some cellular division processes. As a result, the anti-tumor compounds produced using this method are cytostatic or cytotoxic to all dividing cells, even normal cells, and hence are nonspecific [(171)].

Because of their biodegradability, biocompatibility, surface modulation, durability, excellent pharmacokinetic regulation, and suitability for entrapping a broad variety of therapeutic agents, nanoparticle-targeting anti-cancer drugs have lately been given further consideration [(172)].

3.4.2 Cytotoxicity by MTT assay

The MTT assay is a swift colorimetric assay designed for cell viability high testing in a 96-well design. This assay measures reduction of yellow MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) to an insoluble blue formazan substance by mitochondrial succinate dehydrogenase. When cells die, they lose their ability to transform MTT into formazan, thus, color formation serves as a sign of the viable cells [(173)].

The cytotoxicity of platinum nanoparticles synthesized by zahidi and khastawi dates extract were investigated by MTT method for 72 hours in this study using the abnormal cell lines of SKO-3 Ovarian cancer cell line and SK-GT-4 Oesophageal cancer cell line.

The human SKO-3 Ovarian cancer cell line and SK-GT-4 Oesophageal cancer cell line were exposed to PtNPs at different concentrations to determine the anti-proliferative influence.

The cytotoxic effect of PtNPs on the human cancer cell lines SKO-3 and SK-GT-4 after 72 hours were examined. The results showed significant inhibition of cell proliferation in cell lines. Furthermore, the inhibition of cell proliferation was significantly increased depending on concentration, as shown in Figures (3-10), (3-11), (3-12) and (3-13). The different concentrations of PtNPs used are as follows: (0.00125, 0.0025, 0.005 and 0.01) M .

The results indicated that PtNPs are considered to be a precious source of effective anti-proliferative and cytotoxic substances. PtNPs have also been reported to move across cell membranes and interfere with cellular structures, implying that it has a significant effect on cell activity and viability. These results agree with Bendale, *et.al* [(174)].

The inhibition rate of PtNPs in SKO-3 and SK-GT-4 cells at different concentrations of PtNPs used in this study are shown in Tables (3-2) and (3-3).

Table (3-2): Inhibition rate of PtNPs synthesized by zahidi dates extract

Concentration	Inhibition rate on SKO-3 cell line %	Inhibition rate on SK-GT-4 cell line %
0.00125 M	12.5%	20%
0.0025 M	26%	34%
0.005 M	63%	70%
0.01 M	75%	78%

Table (3-3):Inhibition rate of PtNPs synthesized by khastawi dates extract

Concentration	Inhibition rate on SKO-3 cell line %	Inhibition rate on SK-GT-4 cell line %
0.00125 M	13%	17.5%
0.0025 M	28%	28%
0.005 M	64%	68%
0.01 M	76%	77%

Alshatwi, *et.al*, (2015) [175] and Şahin, *et.al*, (2018) [176] demonstrated that platinum nanoparticles were a significant cytotoxic effect on abnormal cells. As a result, these nanoparticles may be used as part of the research and development process for effective anti-cancer therapeutics.

The apoptosis property was also investigated through morphological changes in SKO-3 and SK-GT-4 cell lines. The control (untreated) cells showed that the treated cells maintained their original morphology form. By contrast, SKO-3 and SK-GT-4 cell lines treated with PtNPs showed changes in morphology. The toxicity was increased due to the reduction in the number of SKO-3 and SK-GT-4 cell colonies in those treated with the PtNPs, thereby indicating strong cell-killing as shown in Figures (3-14) and (3-15).

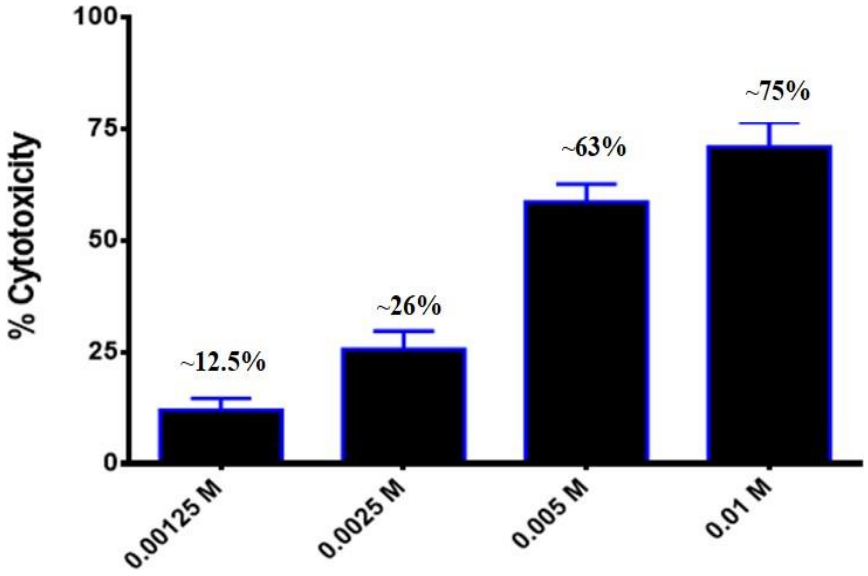


Figure (3-10): Cytotoxic effect of zahidi PtNPs in SKO-3 cell line.

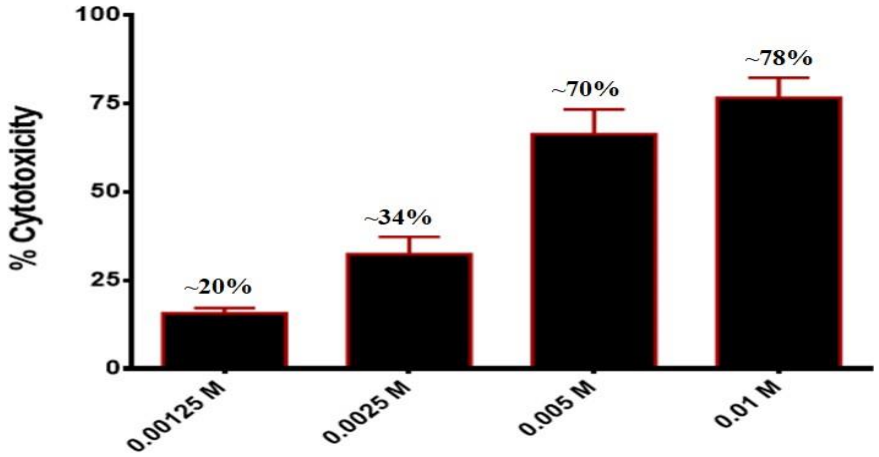


Figure (3-11): Cytotoxic effect of zahidi PtNPs in SK-GT-4 cell line.

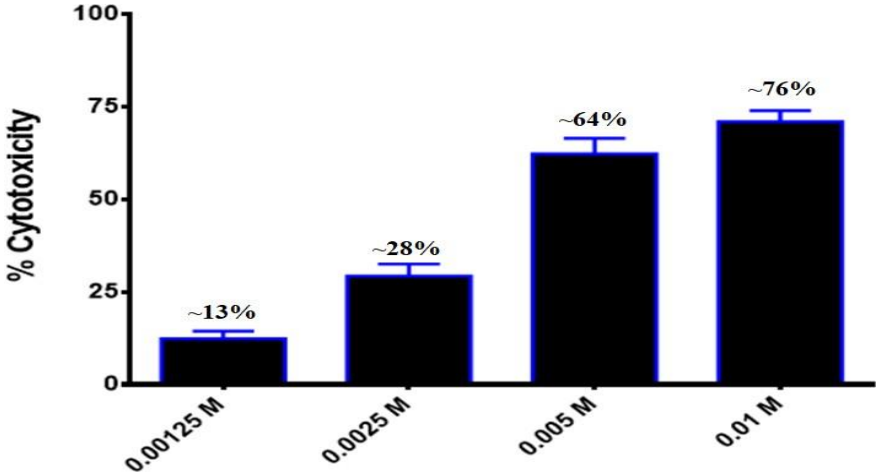


Figure (3-12): Cytotoxic effect of khastawi PtNPs in SKO-3 cell line.

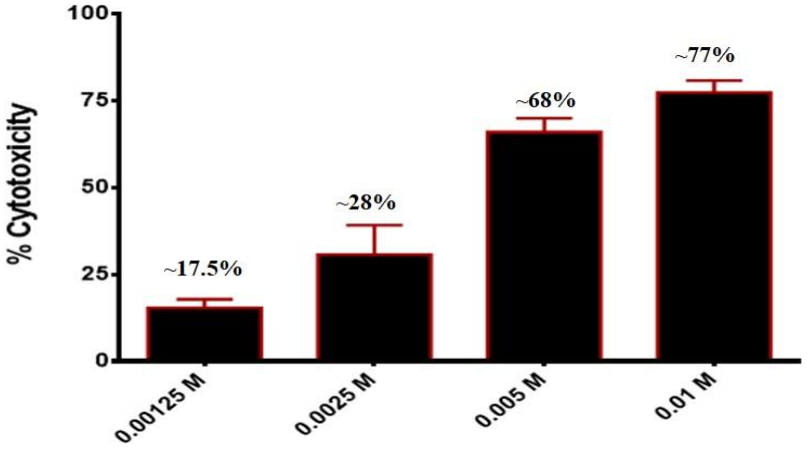


Figure (3-13):Cytotoxic effect of khastawi PtNPs in SK-GT-4 cell line.

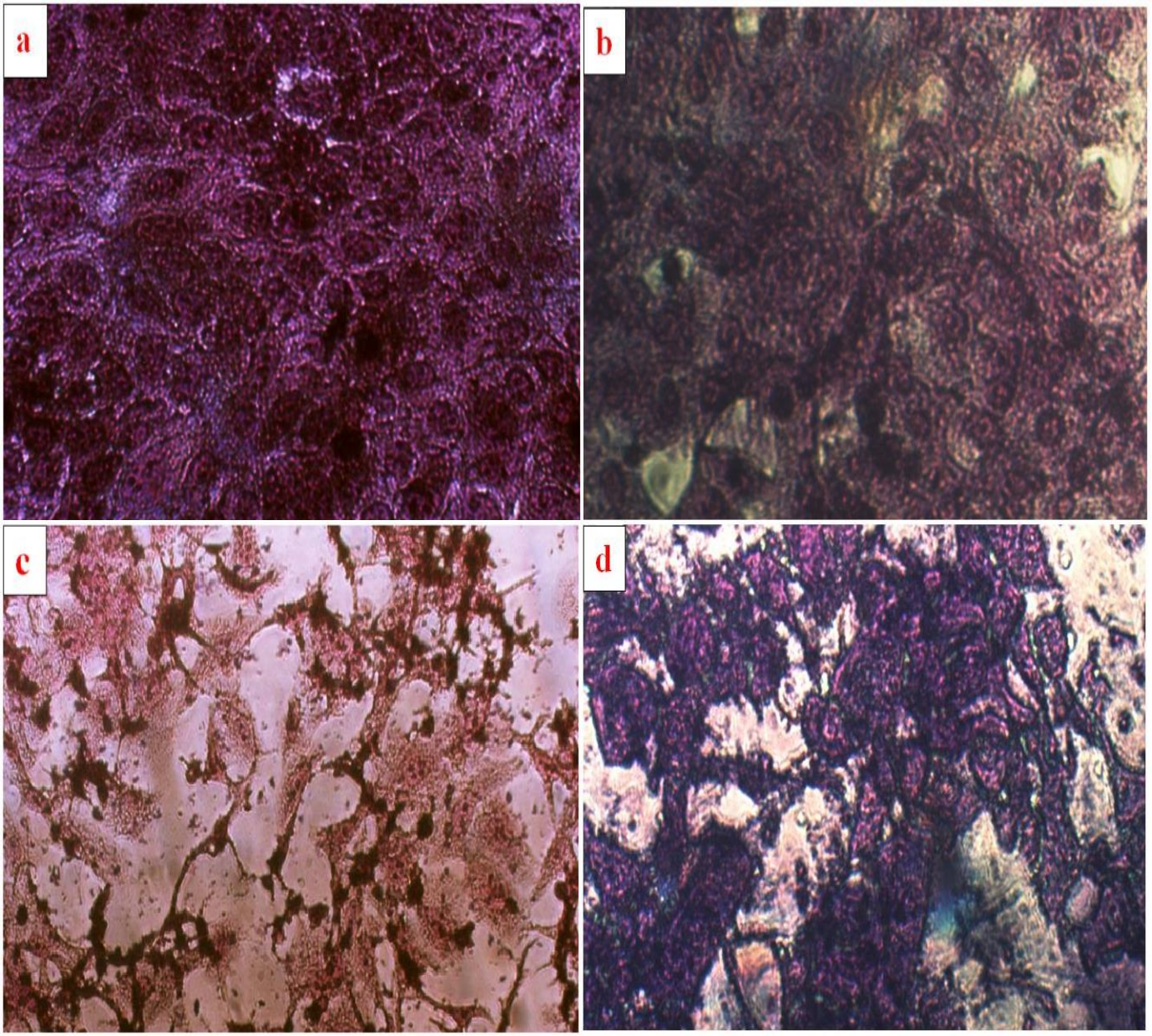


Figure (3-14): (a). Control untreated SKO-3 cells

3.4.2.1 Control untreated SK-GT-4 cells

3.4.2.2 Morphological changes in SKO-3 cell line after treated with zahidi PtNPs. (d). Morphological changes in SK-GT-4 cell line after treated with zahidi PtNPs.

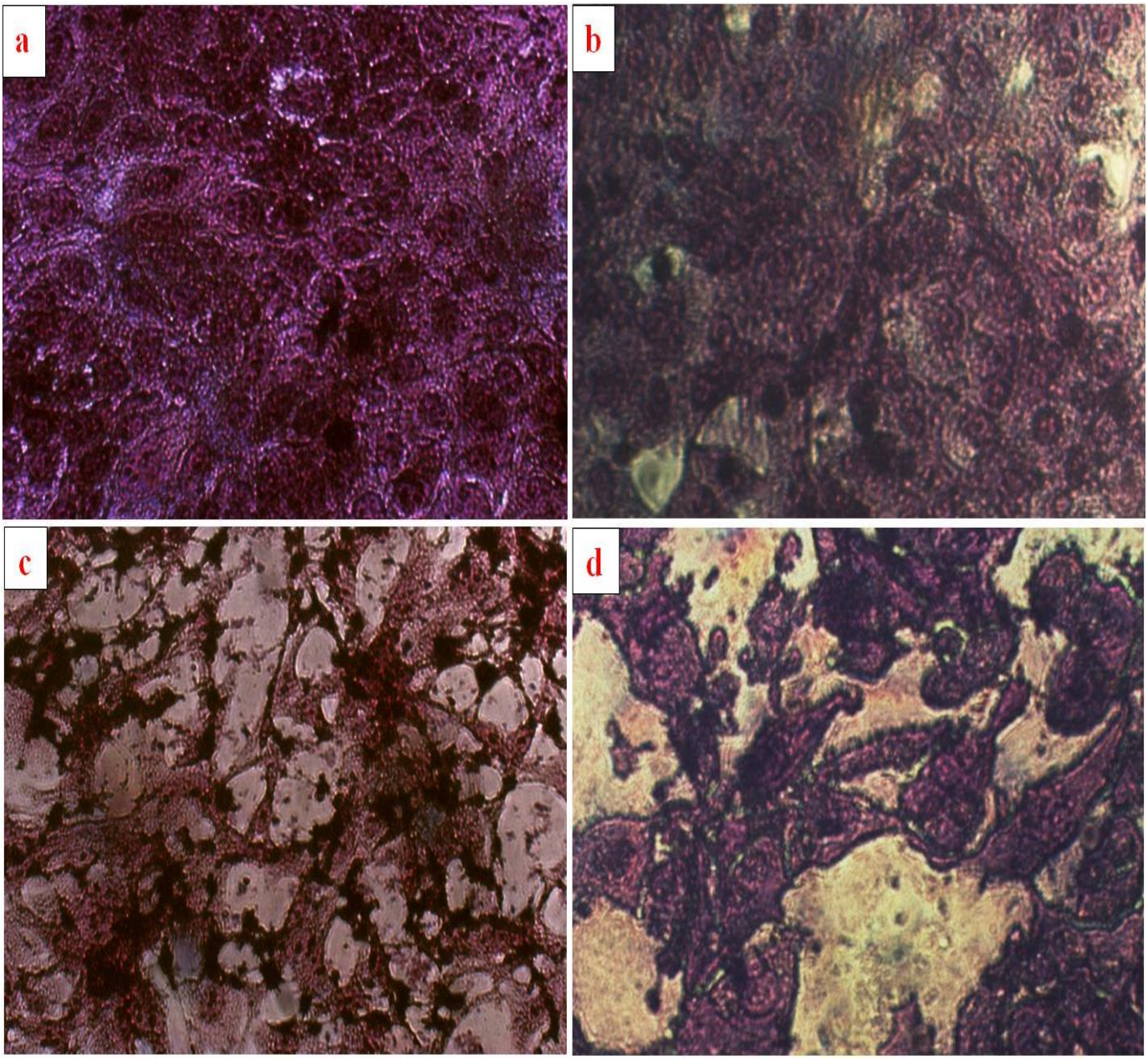


Figure (3-15): (a). Control untreated SKO-3 cells
(b). Control untreated SK-GT-4 cells
(c). Morphological changes in SKO-3 cell line after treated with khastawi PtNPs
(d). Morphological changes in SK-GT-4 cell line after treated with khastawi PtNPs

3.4.3 Anti-bacterial activity

The treatment options for treating infections are rapidly restricted due to anti-bacterial resistance, raising the morbidity and mortality associated with infectious diseases induced by bacteria. The production of metal nanoparticles with anti-bacterial activity is an additional approach to combat infections caused by anti-biotic resistant bacteria [177].

The antibacterial activity of PtNPs was tested against Gram-negative bacterial strain *P. aeruginosa* and Gram-positive bacterial strain *S. pyogenes* bacteria. It was found that these nanoparticles have great anti-bacterial activity.

3.4.4 Agar well diffusion method

The influence of PtNPs as anti-bacterial drugs was estimated via the agar-well diffusion technique. Gram-negative bacterial strain *P. aeruginosa* and Gram-positive bacterial strain *S. pyogenes* were treated with PtNPs in this study.

Ruiz, *et.al* [178] and Gopal, *et.al* [179] exhibited that the anti-microbial activity of nanoparticles is based on their small size and high surface area. Nanoparticles can penetrate biofilms and bacterial cell walls, affecting intracellular processes because of their large surface area and small size. Several studies focused on the interactions of living cells with PtNPs. The uptake and bioactivity of PtNPs on human cells have also been examined. The PtNPs enter the cells via diffusion and localize within the cytoplasm. DNA damage, cell aggregation, and cell apoptosis were also increased by exposure to PtNPs.

The influence of PtNPs as anti-bacterial drugs was estimated via the agr-well diffution technique. Gram-negative bacterial strain *P. aeruginosa* and Gram-positive bacterial strain *S. pyogenes* bacteria were treated with PtNPs in this study. Different concentrations of PtNPs were added on Gram-negative bacterial strain *P. aeruginosa* and Gram-positive bacterial strain *S. pyogenes* which revealed inhibition zones with different diameters, as shown in Table (3-4) and (3-5).

Table (3-4): Growth inhibition of PtNPs by zahidi dates extract

Concentrations	Inhibition zone mm of *P.aeruginosa*	Inhibition zone mm of *S.pyogenes*
0.00125 M	20 mm	18.2 mm
0.0025 M	24.5 mm	23 mm
0.005 M	26.5 mm	28.4 mm
0.05 M	32.5 mm	35.5 mm

Table (3-5): Growth inhibition of PtNPs by Khastawi dates extract

Concentrations	Inhibition zone mm of *P.aeruginosa*	Inhibition zone mm of *S. pyogenes*
0.00125 M	15 mm	17 mm
0.0025 M	17.5 mm	21mm
0.005 M	24 mm	26 mm
0.05 M	31 mm	33 mm

The influence of PtNPs against *P. aeruginosa* and *S. pyogenes* bacteria at different concentrations showed significant growth inhibition with an increase in dose concentration. As shown in Figures (3-16), (3-17), (3-18) and (3-19). These results agree with Kumar, *et.al* [(180)].

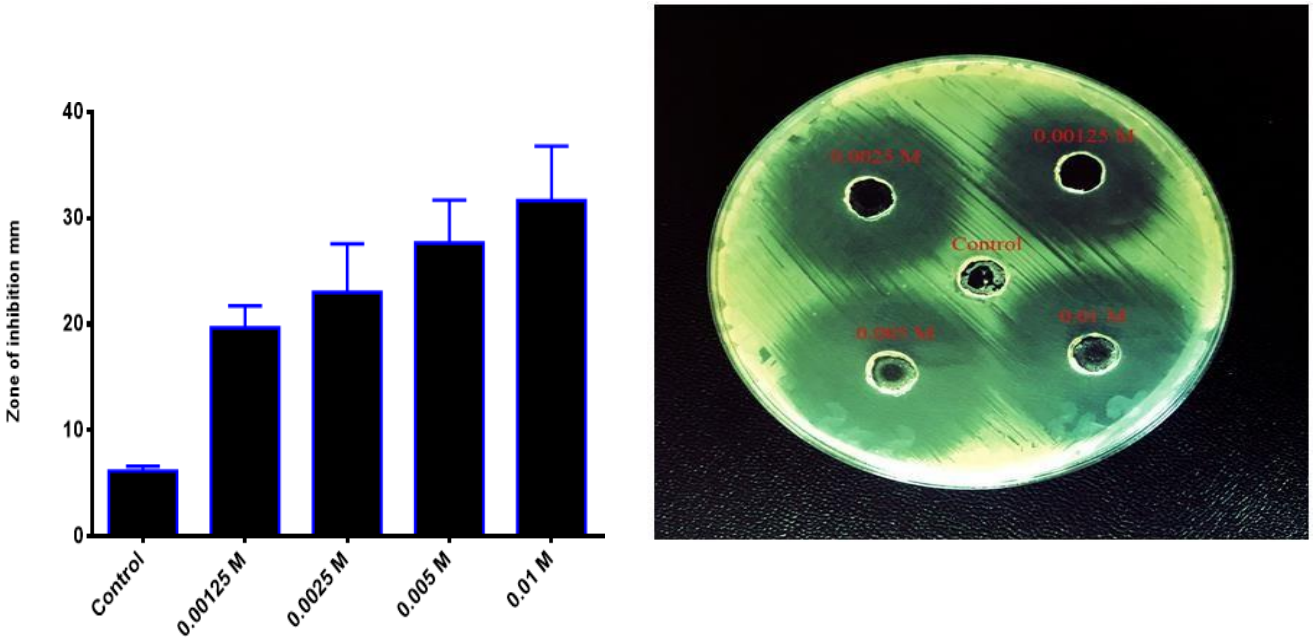


Figure (3-16): Antibacterial activity of zahidi PtNPs against *Pseudomonas aeruginosa*.

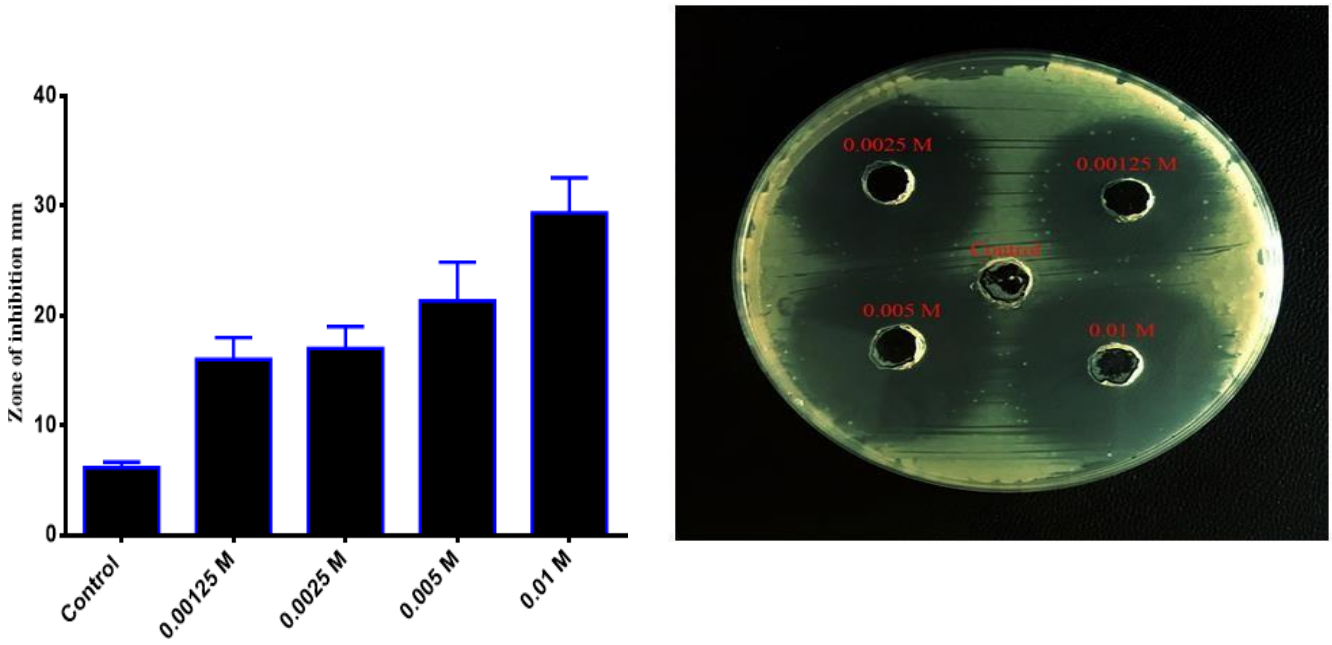


Figure (3-17): Antibacterial activity of khastawi PtNPs against *Pseudomonas aeruginosa*.

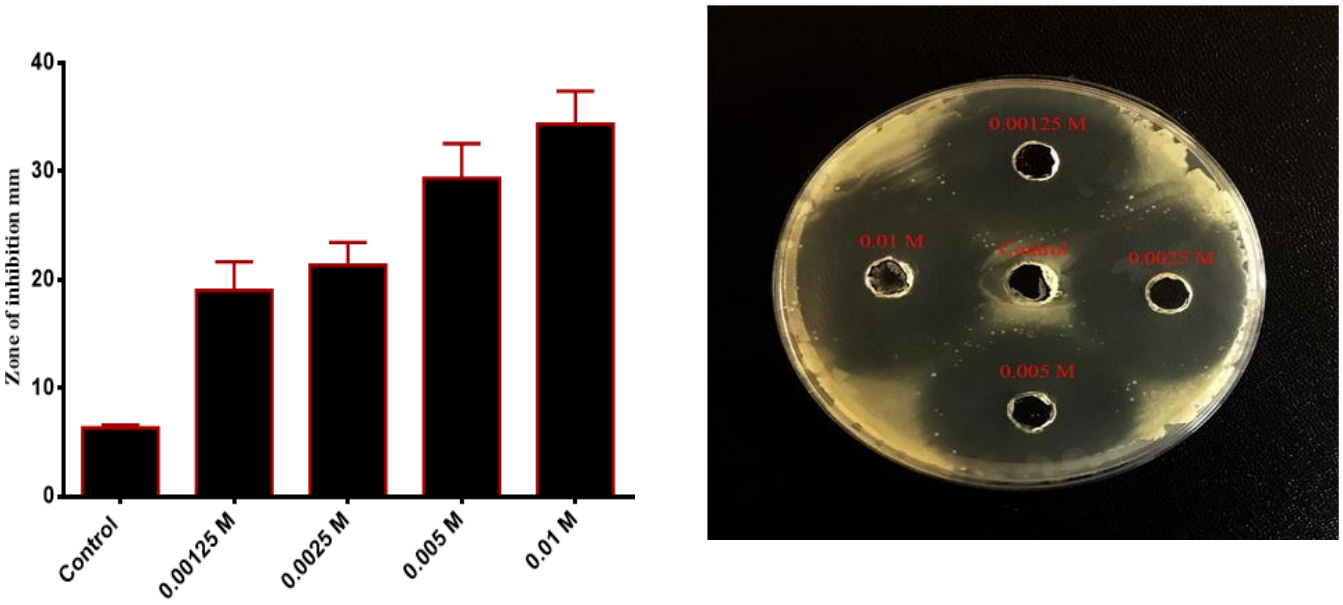


Figure (3-18): Antibacterial activity of zahidi PtNPs against *Streptococcus pyogenes*.

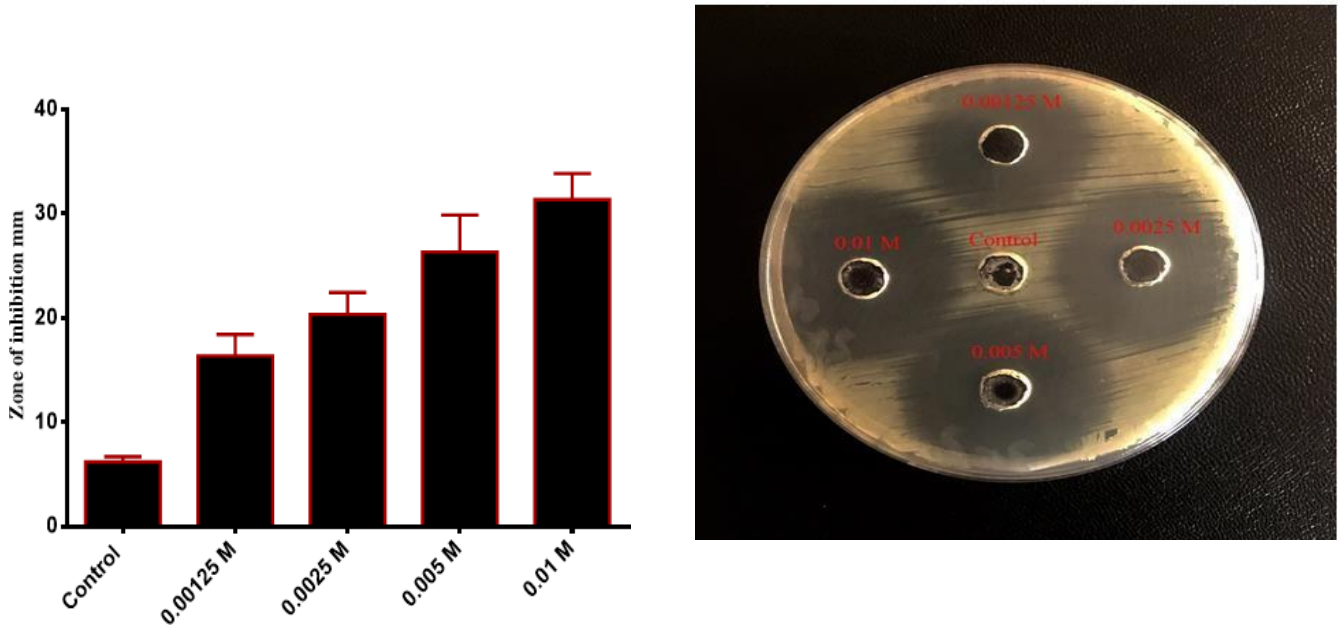


Figure (3-19): Antibacterial activity of khastawi PtNPs against *Streptococcus pyogenes*.

3.5 Conclusions and recommendations

3.5.1 Conclusions

The following conclusions are drawn from this research based on the study's purpose and objectives.

1. Synthesis PtNPs from aqueous solution of date extract of zahidi and khastawi as a possible eco-friendly sustainable bio-resource.
2. Platinum nanoparticles preparation were confirmed by use UV-Vis, FT-IR, XRD, TEM, SEM, and AFM were used to assess the scale, morphology, and form of the PtNPs. UV-Vis research confirmed the formation of PtNPs and confirmed that they were made entirely of pure PtNPs. The average diameter range of the PtNPs was (30 – 40) nm .
3. Bioactive PtNPs activity was capped by zahidi and khastawi dates extract had a high level of cytotoxicity against the Ovarian cancer humans SKO-3 and Oesophageal adenocarcinoma SK-GT-4 cell lines. This supports the theory that PtNPs that have prepared would be successful against cancer humans cell lines.
4. This is the first time that the activity of prepared PtNPs from zahidi and khastawi against these cell lines has been recorded in Iraq. Manufactured PtNPs were discovered to have a high level of action with increasing the PtNPs concentration.
5. Platinum nanoparticles exhibited high anti-bacterial activity against Gram-negative bacteria *Pseudomonas aeruginosa* and Gram-positive bacteria *Streptococcus pyogenes* with increasing the dose concentration.
6. The agar well diffusion method showed that Gram-negative bacteria *Pseudomonas aeruginosa* and Gram-positive bacteria *Streptococcus pyogenes* were influenced and that was clear from the inhibition zones.

3.5.2 Recommendations

These results suggest that more study into the biological pathways behind this activity should be conducted in order to acquire a better understanding of how it works and to determine the possibility of employing this chemical as cancer and bacterial medication:

1. Study the cytotoxic impact of synthesized platinum nanoparticles produced by a green approach on other cancer cell lines and bacteria.
2. To assess if PtNPs have an effective cytotoxic impact on a live system, their in vivo cytotoxic effects should be studied in an animal model.
3. Investigate immunohistochemistry to determine the extent of cancer tissue damage following treatment with synthesized platinum nanoparticles produced using a green method.

References

1. Sharif, A. O., Sanduk, M., and Taleb, H. M., "The date palm and its role in reducing soil salinity and global warming", In *IV International Date Palm Conference*, Vol. 882, 59-64 (2010).
2. Sakr, M. M., Zeid, I. A., Hassan, A. E., Baz, A. G. I. O., and Hassan, W. M., "Identification of some date palm (Phoenix dactylifera) cultivars by fruit characters) cultivars by fruit characters", *Indian Journal of Science and Technology*, Vol. 3(3) (2010).
3. Al-Khayri, J. M., and Naik, P. M., "Date palm micropropagation: Advances and applications", *Ciência e Agrotecnologia*, Vol. 41(4), 347-358 (2017).
4. Zabar, A. F., and Borowy, A., "Cultivation of date palm in Iraq", *Annales Universitatis Mariae Curie-Skłodowska. Sectio EEE, Horticultura*, Vol. 22(1), 39-54 (2012).
5. Al-Alawi, R. A., Al-Mashiqri, J. H., Al-Nadabi, J. S., Al-Shihi, B. I., and Baqi, Y., "Date palm tree (Phoenix dactylifera L.): Natural products and therapeutic options", *Frontiers in plant science*, Vol. 8, 845 (2017).
6. Hussain, M. I., Farooq, M., and Syed, Q. A., "Nutritional and biological characteristics of the date palm fruit (Phoenix dactylifera L.)–A review", *Food Bioscience*, Vol. 34, 100509 (2020).
7. Qadir, A., Shakeel, F., Ali, A., and Faiyazuddin, M., "Phytotherapeutic potential and pharmaceutical impact of Phoenix dactylifera (date palm): current research and future prospects", *Journal of food science and technology*, Vol. 57(4), 1191-1204 (2020).
8. Kuras, M. J., Zielińska-Pisklak, M., Duszyńska, J., and Jabłońska, J., "Determination of the elemental composition and antioxidant properties of dates (Phoenix dactyliferia) originated from different regions", *Journal of food science and technology*, Vol. 57(8), 2828-2839 (2020).
9. Aldulaimi, A. K. O., Idan, A. H., Radhi, A. H., Aowda, S. A., Azziz, S. S. S. A., Salleh, W. M. N. H. W., ... and Ali, N. A. M., "GCMS Analysis and Biological

Activities of Iraq Zahdi Date Palm Phoenix dactylifera L Volatile Compositions", *Research Journal of Pharmacy and Technology*, Vol. 13(11), 5207-5209 (2020).

10. Jain, S. M., and Johnson, D. V. and Al-Khayri. J. M., "Date palm genetic resources and utilization", Africa and the Americas: *Springer*, 1 (2015).
11. Benelmekki, M., "An introduction to nanoparticles and nanotechnology", In *Designing Hybrid Nanoparticles*, *Morgan & Claypool Publishers*, (2015).
12. Pal, S. L., Jana, U., Manna, P. K., Mohanta, G. P., and Manavalan, R., "Nanoparticle: An overview of preparation and characterization", *Journal of applied pharmaceutical science*, Vol. 1(6), 228-234 (2011).
13. Ratner, M. A., and Ratner, D., "Nanotechnology: A gentle introduction to the next big idea", *Prentice Hall Professional*, (2003).
14. Kelley, S., and Sargent, T., "Introduction to Nanotechnology: The new science of small", *Teaching Company*, (2012).
15. Blackman, J., "Metallic nanoparticles", *Elsevier*, (2008).
16. Ramsden, J., "Nanotechnology: an introduction", *William Andrew*, (2016).
17. Srilatha, B., "Nanotechnology in agriculture", *J. Nanomed. Nanotechnol*, Vol. 2(7), 5 (2011).
18. Rogers-Hayden, T., and Pidgeon, N., "Moving engagement "upstream"? nanotechnologies and the royal society and royal academy of engineering's inquiry", *Public Understanding of Science*, Vol. 16(3), 345-364 (2007).
19. Kaya, N., and Karataş, H., "Nanotechnology in the curriculum: A review of the literature", *International Journal of Physics & Chemistry Education*, Vol. 8(2), 49-58 (2016).
20. Vollath, D., "Nanoparticles-nanocomposites–nanomaterials: An introduction for beginners", *John Wiley & Sons*, (2013).
21. Nikalje, A. P., "Nanotechnology and its applications in medicine", *Med chem*, Vol. 5(2), 081-089 (2015).

22. Nasrollahzadeh, M., Sajadi, S. M., Sajjadi, M., and Issaabadi, Z., "Applications of nanotechnology in daily life", *Interface Science and Technology*, Vol. 28, 113-143 (2019).
23. Qu, X., Alvarez, P. J., and Li, Q., "Applications of nanotechnology in water and wastewater treatment", *Water research*, Vol. 47(12), 3931-3946 (2013).
24. Rashidi, L., and Khosravi-Darani, K., "The applications of nanotechnology in food industry", *Critical reviews in food science and nutrition*, Vol. 51(8), 723-730 (2011).
25. Abobatta, W. F., "Nanotechnology application in agriculture", *Acta Scientific Agriculture*, Vol. 2(6), 99-102 (2018).
26. Oluwasanu, A. A., Oluwaseun, F. A., Teslim, J. A., Isaiah, T. T., Olalekan, I. A., and Chris, O. A., "Scientific applications and prospects of nanomaterials: A multidisciplinary review", *African Journal of Biotechnology*, Vol. 18(30), 946-961 (2019).
27. Narayan, R. (Ed.)., "Nanobiomaterials: Nanostructured materials for biomedical applications", *Woodhead Publishing*, (2017).
28. Nouailhat, A., "An introduction to nanoscience and nanotechnology", *John Wiley & Sons*, 10 (2010).
29. Cerjak, H., "Nanomaterials: An introduction to synthesis, properties and applications", *Materials Technology*, Vol. 24(2), 74 (2009).
30. Saleh, T. A., "Nanomaterials: Classification, properties, and environmental toxicities", *Environmental Technology & Innovation*, Vol. 20, 101067 (2020).
31. Jeevanandam, J., Barhoum, A., Chan, Y. S., Dufresne, A., and Danquah, M. K., "Review on nanoparticles and nanostructured materials: History, sources, toxicity and regulations", *Beilstein journal of nanotechnology*, Vol. 9(1), 1050-1074 (2018).
32. Navya, P. N., and Daima, H. K., "Rational engineering of physicochemical properties of nanomaterials for biomedical applications with nanotoxicological perspectives", *Nano Convergence*, Vol. 3(1), 1-14 (2016).

33. Cao, G., "Nanostructures & nanomaterials: Synthesis, properties & applications", *Imperial college press*, (2004).

34. Maiti, D., Tong, X., Mou, X., and Yang, K., "Carbon-based nanomaterials for biomedical applications: a recent study", *Frontiers in pharmacology*, Vol. 9, 1401 (2019).

35. Jeyaraj, M., Gurunathan, S., Qasim, M., Kang, M. H., and Kim, J. H., "A comprehensive review on the synthesis, characterization, and biomedical application of platinum nanoparticles", *Nanomaterials*, Vol. 9(12), 1719 (2019).

36. Kumar, H., Venkatesh, N., Bhowmik, H., and Kuila, A., "Metallic nanoparticle: A review", *Biomedical Journal of Scientific & Technical Research*, Vol. 4(2), 3765-3775 (2018).

37. Begum, R., Ahmad, G., Najeeb, J., Wu, W., Irfan, A., Azam, M., and Farooqi, Z. H., "Stabilization of silver nanoparticles in crosslinked polymer colloids through chelation for catalytic degradation of p-nitroaniline in aqueous medium", *Chemical Physics Letters*, Vol. 763, 138263 (2021).

38. Salem, S. S., and Fouda, A., "Green synthesis of metallic nanoparticles and their prospective biotechnological applications: An overview", *Biological trace element research*, 1-27 (2020).

39. Pandey, P., and Dahiya, M., "A brief review on inorganic nanoparticles", *J Crit Rev*, Vol. 3(3), 18-26 (2016).

40. Chavali, M. S., and Nikolova, M. P., "Metal oxide nanoparticles and their applications in nanotechnology", *SN applied sciences*, Vol. 1(6), 1-30 (2019).

41. Ijaz, I., Gilani, E., Nazir, A., and Bukhari, A., "Detail review on chemical, physical and green synthesis, classification, characterizations and applications of nanoparticles", *Green Chemistry Letters and Reviews*,Vol. 13(3), 223-245 (2020).

42. Saleh, T. A., "Nanomaterials: Classification, properties, and environmental toxicities", *Environmental Technology & Innovation*, 101067 (2020).

43. Kumar, R., and Lal, S., "Synthesis of organic nanoparticles and their applications in drug delivery and food nanotechnology: a review. *J Nanomater Mol Nanotechnol* Vol. 3 (4), 2-11 (2014).

44. Fang, F., Li, M., Zhang, J., and Lee, C. S., "Different strategies for organic nanoparticle preparation in biomedicine", *ACS Materials Letters*, Vol. 2(5), 531-549 (2020).
45. Khalid, K., Tan, X., Mohd Zaid, H. F., Tao, Y., Lye Chew, C., Chu, D. T., ... and Chin Wei, L., "Advanced in developmental organic and inorganic nanomaterial: a review", *Bioengineered*, Vol. 11(1), 328-355 (2020).
46. Hussain, C. M. (Ed.)., "Handbook of functionalized nanomaterials for industrial applications", *Elsevier*, (2020).
47. Poh, T. Y., Ali, N. A. T. B. M., Mac Aogáin, M., Kathawala, M. H., Setyawati, M. I., Ng, K. W., and Chotirmall, S. H., "Inhaled nanomaterials and the respiratory microbiome: clinical, immunological and toxicological perspectives.", *Particle and fibre toxicology*, Vol. 15(1), 1-16 (2018).
48. Hou, H., Shao, G., Yang, W., and Wong, W. Y., "One-dimensional mesoporous inorganic nanostructures and their applications in energy, sensor, catalysis and adsorption", *Progress in Materials Science*, Vol. 113, 100671 (2020).
49. Mao, J., Zhou, T., Zheng, Y., Gao, H., kun Liu, H., and Guo, Z., "Two-dimensional nanostructures for sodium-ion battery anodes", *Journal of Materials Chemistry A*, Vol. 6(8), 3284-3303 (2018).
50. Abdelnour, S. A., Alagawany, M., Hashem, N. M., Farag, M. R., Alghamdi, E. S., Hassan, F. U., ... and Attia, Y. A., "Nanominerals: fabrication methods, benefits and hazards, and their applications in ruminants with special reference to selenium and zinc nanoparticles", *Animals*, Vol. 11(7), 1916 (2021).
51. Osama, E., El-Sheikh, S. M., Khairy, M. H., and Galal, A. A., "Nanoparticles and their potential applications in veterinary medicine", *Journal of Advanced Veterinary Research*, Vol. 10(4), 268-273 (2020).
52. Agarwal, H., Kumar, S. V., and Rajeshkumar, S., "A review on green synthesis of zinc oxide nanoparticles–An eco-friendly approach", *Resource-Efficient Technologies*, Vol. 3(4), 406-413 (2017).

53. Khan, S. H., "Green nanotechnology for the environment and sustainable development", In *Green materials for wastewater treatment*, Vol. 38, 13-46 (2020).
54. Nadaroglu, H., Güngör, A. A., and Selvi, İ. N. C. E., "Synthesis of nanoparticles by green synthesis method", *International Journal of Innovative Research and Reviews*, Vol. 1(1), 6-9 (2017).
55. Bhagyaraj, S. M., Oluwafemi, O. S., Kalarikkal, N., and Thomas, S. (Eds.)., "Synthesis of inorganic nanomaterials: Advances and key technologies", (2018).
56. Singh, J., Singh, T., and Rawat, M., "Green synthesis of silver nanoparticles via various plant extracts for anti-cancer applications", *Nanomedicine*, Vol. 7(3), 1-4 (2017).
57. Nangare, S. N., and Patil, P. O., "Green synthesis of silver nanoparticles: An eco-friendly approach", *Nano Biomedicine & Engineering*,Vol. 12(4), 281-296 (2020).
58. Kanchi, S., & Ahmed, S. (Eds.)., *"Green metal nanoparticles: synthesis, characterization and their applications*", *John Wiley & Sons*, (2018).
59. Devatha, C. P., and Thalla, A. K., "Green synthesis of nanomaterials", In *Synthesis of inorganic nanomaterials*, *Woodhead Publishing*, 169-184 (2018).
60. Verma, A., Gautam, S. P., Bansal, K. K., Prabhakar, N., and Rosenholm, J. M., "Green nanotechnology: Advancement in phytoformulation research", *Medicines*, Vol. 6(1), 39 (2019).
61. Reith, F., Campbell, S. G., Ball, A. S., Pring, A., and Southam, G., "Platinum in earth surface environments", *Earth-Science Reviews*, Vol. 131, 1-21 (2014).
62. Bao, D., "Dynamics and correlation of platinum-group metals spot prices", *Resources Policy*, Vol. 68, 101772 (2020).
63. Cornish, L. A., and Chown, L. H., "Platinum-based alloys and coatings: Materials for the future", *Advances in Gas Turbines*, 337-370 (2011).
64. Colombo, C., Oates, C. J., Monhemius, A. J., and Plant, J. A., "Complexation of platinum, palladium and rhodium with inorganic ligands in the environment", *Geochemistry: Exploration, Environment, Analysis*, Vol. 8(1), 91-101 (2008).

65. Fortin, C., Wang, F., and Pitre, D., "Critical review of platinum group elements (Pd, Pt, Rh) in aquatic ecosystem", (2011).
66. Green, R. A., Toor, H., Dodds, C., and Lovell, N. H., "Variation in performance of platinum electrodes with size and surface roughness", *Sensors and Materials*, Vol. 24(4), 165-180 (2012).
67. Pohan, L. A. G., Kambiré, O., Berté, M., and Ouattara, L., "Study of lifetime of platinum modified metal oxides electrodes", *International Journal of Biological and Chemical Sciences*, Vol. 14(4), 1479-1488 (2020).
68. Ravindra, K., Bencs, L., and Van Grieken, R., "Platinum group elements in the environment and their health risk", *Science of the total environment*, Vol. 318(1-3), 1-43 (2004).
69. Rajendran, S., Prabha, S. S., Rathish, R. J., Singh, G., and Al-Hashem, A., "Antibacterial activity of platinum nanoparticles", In *Nanotoxicity*, *Elsevier*, 275-281 (2020).
70. Czubacka, E., and Czerczak, S., "Are platinum nanoparticles safe to human health?", *Medycyna pracy*, Vol. 70(4), 487-495 (2019).
71. Gholami-Shabani, M., Gholami-Shabani, Z., Shams-Ghahfarokhi, M., Akbarzadeh, A., Riazi, G., and Razzaghi-Abyaneh, M., "Biogenic approach using sheep milk for the synthesis of platinum nanoparticles: The role of milk protein in platinum reduction and stabilization", *International Journal of Nanoscience and Nanotechnology*, Vol. 12(4), 199-206 (2016).
72. Sadrolhosseini, A. R., Habibiasr, M., Shafie, S., Solaimani, H., and Lim, H. N., "Optical and thermal properties of laser-ablated platinum nanoparticles graphene oxide composite", *International journal of molecular sciences*, Vol. 20(24), 6153 (2019).
73. Yusof, F., and Ismail, N. A. S., "Antioxidants effects of platinum nanoparticles: A potential alternative treatment to lung diseases", *J. Appl. Pharm. Sci*, Vol. 5, 140-145 (2015).

74. Jameel, M. S., Aziz, A. A., and Dheyab, M. A., "Green synthesis: Proposed mechanism and factors influencing the synthesis of platinum nanoparticles", *Green Processing and Synthesis*, Vol. 9(1), 386-398 (2020).
75. Tahir, F., Begum, R., Wu, W., Irfan, A., and Farooqi, Z. H., "Physicochemical aspects of inorganic nanoparticles stabilized in N-vinyl caprolactam based microgels for various applications", *RSC Advances*, Vol.11(2), 978-995 (2021).
76. Gautam, A., Guleria, P., and Kumar, V., "Platinum nanoparticles: Synthesis strategies and applications", *Nanoarchitectonics*, 70-86 (2020).
77. Stepanov, A. L., Golubev, A. N., Nikitin, S. I., and Osin, Y. N., "A review on the fabrication and properties of platinum nanoparticles", *Rev. Adv. Mater. Sci*, Vol. 38(2), 160-175 (2014).
78. Zhai, D., Liu, B., Shi, Y., Pan, L., Wang, Y., Li, W., and Yu, G., "Highly sensitive glucose sensor based on Pt nanoparticle/polyaniline hydrogel heterostructures", *ACS nano*, Vol. 7(4), 3540-3546 (2013).
79. Fu, S., Zhu, C., Song, J., Engelhard, M., Xia, H., Du, D., and Lin, Y., "PdCuPt nanocrystals with multibranches for enzyme-free glucose detection", *ACS applied materials & interfaces*, Vol. 8(34), 22196-22200 (2016).
80. Almurshidi, B., "Selenium, platinum and cerium oxide nanoparticles' applications to cancer and fibrotic diseases in medicine", (Doctoral dissertation, University of South Carolina), (2020).
81. Yin, T., Wang, Z., Li, X., Li, Y., Bian, K., Cao, W., and Gao, D., "Biologically inspired self-assembly of bacitracin-based platinum nanoparticles with anti-tumor effects", *New Journal of Chemistry*, Vol. 41(8), 2941-2948 (2017).
82. Yamada, M., Foote, M., and Prow, T. W., "Therapeutic gold, silver, and platinum nanoparticles", *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, Vol. 7(3), 428-445 (2015).
83. Daneshvar, F., Salehi, F., Karimi, M., Vais, R. D., Mosleh-Shirazi, M. A., and Sattarahmady, N., "Combined X-ray radiotherapy and laser photothermal therapy of melanoma cancer cells using dual-sensitization of platinum

nanoparticles", *Journal of Photochemistry and Photobiology B: Biology*, Vol. 203, 111737 (2020).

84. Puja, P., and Kumar, P., "A perspective on biogenic synthesis of platinum nanoparticles and their biomedical applications", *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Vol. 211, 94-99 (2019).

85. Beyth, N., Houri-Haddad, Y., Domb, A., Khan, W., and Hazan, R., "Alternative antimicrobial approach: nano-antimicrobial materials", *Evidence-based complementary and alternative medicine*, Vol. 2015, 1-16 (2015).

86. Salem, H., Attiya, G., and El-Fishawy, N., "Classification of human cancer diseases by gene expression profiles", *Applied Soft Computing*, Vol. 50, 124-134 (2017).

87. Hassanpour, S. H., and Dehghani, M., "Review of cancer from perspective of molecular", *Journal of Cancer Research and Practice*, Vol. 4(4), 127-129 (2017).

88. Ruddon, R. W., "Cancer biology", *Oxford University Press*, (2007).

89. Saini, K. S., Tagliamento, M., Lambertini, M., McNally, R., Romano, M., Leone, M., and de Azambuja, E., "Mortality in patients with cancer and coronavirus disease 2019: A systematic review and pooled analysis of 52 studies", *European Journal of Cancer*, Vol. 139, 43-50 (2020).

90. Marmot, M., Atinmo, T., Byers, T., Chen, J., Hirohata, T., Jackson, A., and Zeisel, S., "Food, nutrition, physical activity, and the prevention of cancer: A global perspective", (2007).

91. Hannoodee, S., and Nasuruddin, D. N., "Acute inflammatory response", *StatPearls [Internet]*, (2020).

92. Karlsson, T., Johansson, T., Höglund, J., Ek, W. E., and Johansson, Å., "Time-Dependent Effects of Oral Contraceptive Use on Breast, Ovarian, and Endometrial Cancers", *Cancer Research*, Vol. 81(4), 1153-1162 (2021).

93. Bozzone, D. M., "Causes of cancer the biology of cancer", *Chelsea House*, 126 (2007).

94. Ahmad, I. M., Abdalla, M. Y., Moore, T. A., Bartenhagen, L., Case, A. J., and Zimmerman, M. C., "Healthcare workers occupationally exposed to ionizing

radiation exhibit altered levels of inflammatory cytokines and redox parameters", *Antioxidants*, Vol. 8(1), 12 (2019).

95. Tanguler, H., and Kabak, B., "Chemical hazards in foods", In *Health and Safety Aspects of Food Processing Technologies*, Springer ,Cham. , 349-402 (2019).
96. Awuchi, C. G., Amagwula, I. O., Priya, P., Kumar, R., Yezdani, U., and Khan, M. G., "Aflatoxins In Foods And Feeds: A Review On Health Implications, Detection, And Control", *Bull. Environ. Pharmacol. Life Sci*, Vol. 9, 149-155 (2020).
97. Kunnumakkara, A. B., "Anticancer properties of fruits and vegetables: A scientific review", *World Scientific*, (2014).
98. Robak, P., Drozdz, I., Szemraj, J., and Robak, T., "Drug resistance in multiple myeloma", *Cancer treatment reviews*, Vol. 70, 199-208 (2018).
99. Matsui, W., Huff, C. A., Wang, Q., Malehorn, M. T., Barber, J., Tanhehco, Y., and Jones, R. J., "Characterization of clonogenic multiple myeloma cells", *Blood*, Vol. 103(6), 2332-2336 (2004).
100. Derksen, P. W., Tjin, E., Meijer, H. P., Klok, M. D., Mac Gillavry, H. D., van Oers, M. H., and Pals, S. T., "Illegitimate WNT signaling promotes proliferation of multiple myeloma cells", *Proceedings of the National Academy of Sciences*, Vol. 101(16), 6122-6127 (2004).
101. Sudhakar, A., "History of cancer, ancient and modern treatment methods", *Journal of cancer science & therapy*, Vol. 1(2), 1-7 (2009).
102. Cho, K. R., and Shih, I. M., "Ovarian cancer", *Annual review of pathology: mechanisms of disease*, Vol. 4, 287-313 (2009).
103. Stewart, C., Ralyea, C., and Lockwood, S., "Ovarian cancer: An integrated review", In *Seminars in oncology nursing*, *WB Saunders*, Vol. 35(2), 151-156 (2019).
104. Prat, J., "Ovarian carcinomas: Five distinct diseases with different origins, genetic alterations, and clinicopathological features", *Virchows Archiv*, Vol. 460(3), 237-249 (2012).

105. Sahu, L., "Ovarian cancer", *Evidence Based Clinical Gynecology*, 297-305 (2017).
106. Chan, K. K., Siu, M. K., Jiang, Y. X., Wang, J. J., Wang, Y., Leung, T. H., and Ngan, H. Y., "Differential expression of estrogen receptor subtypes and variants in ovarian cancer: Effects on cell invasion, proliferation and prognosis", *BMC cancer*, Vol. 17(1), 1-11 (2017).
107. Wong, M. C., Hamilton, W., Whiteman, D. C., Jiang, J. Y., Qiao, Y., Fung, F. D., and Sung, J. J., "Global incidence and mortality of oesophageal cancer and their correlation with socioeconomic indicators temporal patterns and trends in 41 countries", *Scientific reports*, Vol. 8(1), 1-13 (2018).
108. Lagergren, J., Smyth, E., Cunningham, D., and Lagergren, P., "Oesophageal cancer", *The Lancet*, Vol. 390(10110), 2383-2396 (2017).
109. Xie, S. H., and Lagergren, J., "Risk factors for oesophageal cancer", *Best Practice & Research Clinical Gastroenterology*, Vol. 36, 3-8 (2018).
110. Enzinger, P. C., and Mayer, R. J., "Esophageal cancer", *New England Journal of Medicine*, Vol. 349(23), 2241-2252 (2003).
111. Guinan, E. M., Doyle, S. L., Bennett, A. E., O'Neill, L., Gannon, J., Elliott, J. A., and Hussey, J., "Sarcopenia during neoadjuvant therapy for oesophageal cancer: Characterising the impact on muscle strength and physical performance", *Supportive Care in Cancer*, Vol. 26(5), 1569-1576 (2018).
112. Abbas, G., and Krasna, M., "Overview of esophageal cancer", *Annals of cardiothoracic surgery*, Vol. 6(2), 131-136 (2017).
113. Tang, Y. W., and Sails, A. (Eds.)., "Molecular medical microbiology", *Academic press*, (2014).
114. Angst, D. C., Tepekule, B., Sun, L., Bogos, B., and Bonhoeffer, S., "Comparing treatment strategies to reduce antibiotic resistance in an in vitro epidemiological setting", *Proceedings of the National Academy of Sciences*, Vol. 118(13), 1-7 (2021).
115. Panawala, L., "Difference between gram positive and gram negative bacteria", *Epedıaa* ,Vol. 3 , 1-13 (2017).

116. David, S. M., Jayaprakash, C., and Mathew, A., "Isolation, identification and antibiotic susceptibility testing of pseudomonas aeruginosa and acinetobacter baumannii from endotracheal secretions in a tertiary care centre", *Int. J. Curr. Microbiol. App. Sci*, Vol. 9(2), 1566-1574 (2020).
117. Lalucat, J., Mulet, M., Gomila, M., and García-Valdés, E., "Genomics in bacterial taxonomy: Impact on the genus Pseudomonas", *Genes*, Vol. 11(2), 1-17 (2020).
118. Moore, E. B., Tindall, B., Martins Dos Santos, V. A. P., Pieper, D., Ramos, J. L., and Palleroni, N., "Nonmedical: Pseudomonas", *The prokaryotes*, Vol. 6, 646-703 (2006).
119. Carriel, D., ″Structure-function relationships of the lysine decarboxylase from Pseudomonas aeruginosa ", (Doctoral dissertation, Université Grenoble Alpes), (2017).
120. Pachori, P., Gothalwal, R., and Gandhi, P., "Emergence of antibiotic resistance Pseudomonas aeruginosa in intensive care unit; a critical review", *Genes & diseases*, Vol. 6(2), 109-119 (2019).
121. Alhazmi, A., "Pseudomonas aeruginosa-pathogenesis and pathogenic mechanisms", *International Journal of Biology*, Vol. 7(2), 44-67 (2015).
122. Nulens, E., Gonzalo Bearman, M. D., and Fshea, F., "Guide to infection control in the hospital", *International society for infectious diseases*, (2018).
123. Vos, P., Garrity, G., Jones, D., Krieg, N. R., Ludwig, W., Rainey, F. A., and Whitman, W. B. (Eds.)., "Bergey's manual of systematic bacteriology: Volume 3: The firmicutes", *Science & Business Media*, Vol. 3 (2011).
124. Stevens, D. L., Stevens, D. L., and Kaplan, E. L. (Eds.)., ″Streptococcal infections: Clinical aspects, microbiology, and molecular pathogenesis.", *Oxford University Press, USA*, (2000).
125. AL-Taei, F. A., Al-Khafaji, J. K., and Al-Gazally, M. E., "Characterization of streptococcus pyogenes isolated from throat swabs in Baghdad children patients", *Journal of University of Babylon*, Vol. 24(5), 1227-1233 (2016).

126. Blagden, S., Watts, V., Verlander, N. Q., and Pegorie, M., "Invasive group a streptococcal infections in north west England: Epidemiology, risk factors and fatal infection", *Public Health*, Vol. 186, 63-70 (2020).
127. Osowicki, J., Azzopardi, K. I., Baker, C., Waddington, C. S., Pandey, M., Schuster, T., and Steer, A. C., "Controlled human infection for vaccination against Streptococcus pyogenes (CHIVAS): Establishing a group A Streptococcus pharyngitis human infection study", *Vaccine*, Vol. 37(26), 3485-3494 (2019).
128. Ullah, S., Ahmad, A., Wang, A., Raza, M., Jan, A. U., Tahir, K., and Qipeng, Y., "Bio-fabrication of catalytic platinum nanoparticles and their in vitro efficacy against lungs cancer cells line (A549)", *Journal of Photochemistry and Photobiology B: Biology*, Vol. 173, 368-375 (2017).
129. Tahir, K., Nazir, S., Ahmad, A., Li, B., Khan, A. U., Khan, Z. U. H., and Rahman, A. U., "Facile and green synthesis of phytochemicals capped platinum nanoparticles and in vitro their superior antibacterial activity", *Journal of Photochemistry and Photobiology B: Biology*, Vol. 166, 246-251 (2017).
130. Rokade, S. S., Joshi, K. A., Mahajan, K., Tomar, G., Dubal, D. S., Singh, V., and Ghosh, S., "Novel anticancer platinum and palladium nanoparticles from barleria prionitis", *Global Journal of Nanomedicine*, Vol. 2(5), 555600 (2017).
131. Ramkumar, V. S., Pugazhendhi, A., Prakash, S., Ahila, N. K., Vinoj, G., Selvam, S., and Rajendran, R. B., "Synthesis of platinum nanoparticles using seaweed padina gymnospora and their catalytic activity as PVP/PtNPs nanocomposite towards biological applications", *Biomedicine & Pharmacotherapy*, Vol. 92, 479-490 (2017).
132. Jeyapaul, U., Kala, M. J., Bosco, A. J., Piruthiviraj, P., and Easuraja, M., "An eco-friendly approach for synthesis of platinum nanoparticles using leaf extracts of Jatropa gossypifolia and Jatropa glandulifera and its antibacterial activity", *Oriental Journal of Chemistry*, Vol. 34(2), 783-790 (2018).
133. Almeer, R. S., Ali, D., Alarifi, S., Alkahtani, S., and Almansour, M., "Green platinum nanoparticles interaction with HEK293 cells: Cellular toxicity,

apoptosis, and genetic damage", *Dose-Response*, Vol. 16(4), 1559325818807382 (2018).

134. Gurunathan, S., Jeyaraj, M., Kang, M. H., and Kim, J. H., "The effects of apigenin-biosynthesized ultra-small platinum nanoparticles on the human monocytic THP-1 cell line", *Cells*, Vol. 8(5), 1-23 (2019).
135. Al-Radadi, N. S., "Green synthesis of platinum nanoparticles using Saudi's dates extract and their usage on the cancer cell treatment", *Arabian journal of chemistry*, Vol. 12(3), 330-349 (2019).
136. Aygun, A., Gülbagca, F., Ozer, L. Y., Ustaoglu, B., Altunoglu, Y. C., Baloglu, M. C., and Sen, F., "Biogenic platinum nanoparticles using black cumin seed and their potential usage as antimicrobial and anticancer agent", *Journal of pharmaceutical and biomedical analysis*, Vol. 179, 112961 (2020).
137. Selvi, A. M., Palanisamy, S., Jeyanthi, S., Vinosha, M., Mohandoss, S., Tabarsa, M., and Prabhu, N. M., "Synthesis of tragia involucrata mediated platinum nanoparticles for comprehensive therapeutic applications: Antioxidant, antibacterial and mitochondria-associated apoptosis in HeLa cells", *Process Biochemistry*, Vol. 98, 21-33 (2020).
138. Gurunathan, S., Jeyaraj, M., Kang, M. H., and Kim, J. H., "Anticancer properties of platinum nanoparticles and retinoic acid: Combination therapy for the treatment of human neuroblastoma cancer", *International journal of molecular sciences*, Vol. 21(18), 1-32 (2020).
139. Mohammadlou, M., Maghsoudi, H., and Jafarizadeh-Malmiri, H. J., "A review on green silver nanoparticles based on plants: Synthesis, potential applications and eco-friendly approach", *International Food Research Journal*, Vol. 23(2), 446-463 (2016).
140. Murty, B. S., Shankar, P., Raj, B., Rath, B. B., and Murday, J., "Textbook of nanoscience and nanotechnology.", *Springer Science & Business Media*, (2013).
141. Popelka, A., Zavahir, S., and Habib, S., "Morphology analysis", In *Polymer Science and Innovative Applications*, *Elsevier*, 21-68 (2020).

142. Kumar, C. G., Pombala, S., Poornachandra, Y., and Agarwal, S. V., "Synthesis, characterization, and applications of nanobiomaterials for antimicrobial therapy", In *Nanobiomaterials in Antimicrobial Therapy*, *William Andrew Publishing*, 103-152 (2016).
143. Mudalige, T., Qu, H., Van Haute, D., Ansar, S. M., Paredes, A., and Ingle, T., "Characterization of nanomaterials: Tools and challenges.", *Nanomaterials for Food Applications*, 313-353 (2019).
144. Lin, P. C., Lin, S., Wang, P. C., and Sridhar, R., "Techniques for physicochemical characterization of nanomaterials.", *Biotechnology advances*, Vol. 32(4), 711-726 (2014).
145. Salame, P. H., Pawade, V. B., and Bhanvase, B. A., "Characterization tools and techniques for nanomaterials.", In *Nanomaterials for Green Energy Elsevier*, 83-111 (2018).
146. Khashan, K. S., Sulaiman, G. M., Hussain, S. A., Marzoog, T. R., and Jabir, M. S., "Synthesis, characterization and evaluation of anti-bacterial, anti-parasitic and anti-cancer activities of aluminum-doped zinc oxide nanoparticles", *Journal of Inorganic and Organometallic Polymers and Materials*, 1-17, (2020).
147. Ali, Z., Jabir, M., and Al-Shammari, A., "Gold nanoparticles inhibiting proliferation of human breast cancer cell line", *Research Journal of Biotechnology*, Vol.14, 79-82 (2019).
148. Al-Salman, H. N. K., Ali, E. T., Jabir, M., Sulaiman, G. M., and Al-Jadaan, S. A., "2-Benzhydrylsulfinyl-N-hydroxyacetamide-Na extracted from fig as a novel cytotoxic and apoptosis inducer in SKOV-3 and AMJ-13 cell lines via P53 and caspase-8 pathway", *European Food Research and Technology*, Vol. 246, 1591-1608 (2020).
149. Jabir, M. S., Nayef, U. M., Abdulkadhim, W. K., and Sulaiman, G. M., "Supermagnetic Fe_3O_4-PEG nanoparticles combined with NIR laser and alternating magnetic field as potent anti-cancer agent against human ovarian cancer cells", *Materials Research Express*, Vol.6 (11), 115412-115423, (2019).

150. Al-Ziaydi, A. G., Al-Shammari, A. M., Hamzah, M. I., Kadhim, H. S., and Jabir, M. S., "Newcastle disease virus suppress glycolysis pathway and induce breast cancer cells death", *Virus Disease*, Vol. 5, 1-8, (2020).
151. Khashan, K. S., Jabir, M. S., and Abdulameer, F. A., "Carbon nanoparticles prepared by laser ablation in liquid environment", *Surface Review and Letters*, Vol. 26 (10), 1950078-1950086 (2019).
152. Kareem, S. H., Naji, A. M., Taqi, Z. J., and Jabir, M. S., "Polyvinyl pyrrolidone loaded-Mn-Zn Fe_2O_4 Magnetic nano-composites induce apoptosis in cancer cells through mitochondrial damage and P53 pathway", *Journal of Inorganic and Organometallic Polymers and Materials*, 1-15, (2020).
153. Albukhaty, S., Naderi-Manesh, H., Tiraihi, T., and Sakhi J., M., "Poly-l-lysine coated super paramagnetic nanoparticles: A novel method for the transfection of pro-BDNF into neural stem cells", *Artificial Cells, Nanomedicine, and Biotechnology*, 46 (sup3), S125-S132, (2018).
154. Waheeb, H. M., Sulaiman, G. M., and Jabir, M. S., "Effect of hesperidin conjugated with golden nanoparticles on phagocytic activity: In vitro study", *In AIP Conference Proceedings*, Vol. 2213, (1), 020217-020222 (2020).
155. Al-Shammari, A. M., Al-Saadi, H., Al-Shammari, S. M., and Jabir, M. S., "Galangin enhances gold nanoparticles as anti-tumor agents against ovarian cancer cells", *In AIP Conference Proceedings*, Vol. 2213 (1), 020206-020211 (2020).
156. Kadhim, W. K. A., Nayef, U. M., and Jabir, M. S., "Polyethylene glycol-functionalized magnetic (Fe_3O_4) nanoparticles: A good method for a successful antibacterial therapeutic agent via damage DNA molecule", *Surface Review and Letters (SRL)*, Vol. 26 (10), 1-15, (2019).
157. Jabir, M. S., Nayef, U. M., Jawad, K. H., Taqi, Z. J., and Ahmed, N. R., "Porous silicon nanoparticles prepared via an improved method: A developing strategy for a successful antimicrobial agent against Escherichia coli and Staphylococcus aureus", *In IOP Conference Series: Materials Science and Engineering*, Vol. 454(1), 012077-012084 (2018).

158. Mohammed, M. K. A., Mohammad, M. R., Jabir, M. S., and Ahmed, D. S., "Functionalization, characterization, and antibacterial activity of single wall and multi wall carbon nanotubes", *MS & E*, Vol. 757 (1), 177-183 (2020).
159. Khashan, K. S., Abdulameer, F. A., Jabir, M. S., Hadi, A. A., and Sulaiman, G. M., "Anticancer activity and toxicity of carbon nanoparticles produced by pulsed laser ablation of graphite in water", Advances in Natural Sciences: Nanoscience and Nanotechnology, Vol. 11(3), 035010 (2020).
160. Sameen, A. M., Jabir, M. S., and Al-Ani, M. Q., "Therapeutic combination of gold nanoparticles and LPS as cytotoxic and apoptosis inducer in breast cancer cells", In AIP Conference Proceedings AIP Publishing LLC, Vol. 2213(1), 020215 (2020).
161. Kulkarni, V., Palled, V., Hiregoudar, S., Prakash, K., Maski, D., and Lendra, S., "Bio-synthesis and characterization of titanium dioxide nanoparticles (TiO_2) using azadirachta indica leaf (neem leaf) extract", *Int. J. Curr. Microbiol. Appl. Sci*, Vol. 8, 2309-2317 (2019).
162. Vinayagam, R., Zhou, C., Pai, S., Varadavenkatesan, T., Narasimhan, M. K., Narayanasamy, S., and Selvaraj, R., "Structural characterization of green synthesized magnetic mesoporous Fe_3O_4NPs@ ME", Materials Chemistry and Physics, Vol. 262, 124323 (2020).
163. Malatjie, S. T., "Phytochemical synthesis and characterization of bioactive gold and platinum nanoparticles using hypaphorine and their cytotoxic effects towards HCT 116 human colorectal cancer-derived cells", (Doctoral dissertation, University of Johannesburg), (2017).
164. Dobrucka, R., "Synthesis and structural characteristic of platinum nanoparticles using herbal bidens tripartitus extract", *Journal of Inorganic and Organometallic Polymers and Materials*, Vol. 26(1), 219-225 (2016).
165. Dobrucka, R., Romaniuk-Drapała, A., and Kaczmarek, M., "Evaluation of biological synthesized platinum nanoparticles using ononidis radix extract on the cell lung carcinoma A549", *Biomedical microdevices*, Vol. 21(3), 1-10 (2019).

166. Song, J. Y., Kwon, E. Y., and Kim, B. S., "Biological synthesis of platinum nanoparticles using Diopyros kaki leaf extract", *Bioprocess and Biosystems Engineering*, Vol. 33(1), 159-164 (2010).
167. Khalil, M. M., Mostafa, Y. M., and Torad, E., "Biosynthesis and characterization of Pt and Au-Pt nanoparticles and their photo catalytic degradation of methylene blue", *Int. J. Adv. Res*, Vol. 2(8), 694-703 (2014).
168. Ismail, E. H., and Al-Radadi, N. S., "An eco-friendly synthesis of platinum nanoparticles and their applications on the cancer cell treatments", *Journal of Computational and Theoretical Nanoscience*, Vol. 14(12), 6044-6052 (2017).
169. Prabhu, N., and Gajendran, T., "Green synthesis of noble metal of platinum nanoparticles from ocimum sanctum (Tulsi) Plant-extracts", *J. Biotechnol. Biochem*, Vol. 3, 107-112 (2017).
170. Das, R., Bee Abd Hamid, S., Eaqub Ali, M., Ramakrishna, S., and Yongzhi, W., "Carbon nanotubes characterization by X-ray powder diffraction–a review", *Current Nanoscience*, Vol. 11(1), 23-35 (2015).
171. Avendaño, C., and Menendez, J. C., "Medicinal chemistry of anticancer drugs", *Elsevier*, (2015).
172. Saeidnia, S., "New approaches to natural anticancer drugs", *Springer International Publishing*, (2015).
173. Karakaş, D., Ari, F., and Ulukaya, E., "The MTT viability assay yields strikingly false-positive viabilities although the cells are killed by some plant extracts", *Turkish Journal of Biology*, Vol. 41(6) , 919-925 (2017).
174. Bendale, Y., Bendale, V., and Paul, S., "Evaluation of cytotoxic activity of platinum nanoparticles against normal and cancer cells and its anticancer potential through induction of apoptosis", *Integrative medicine research*, Vol. 6(2), 141-148 (2017).
175. Alshatwi, A. A., Athinarayanan, J., and Subbarayan, P. V., "Green synthesis of platinum nanoparticles that induce cell death and G2/M-phase cell cycle arrest in human cervical cancer cells", *Journal of Materials Science: Materials in Medicine*, Vol. 26(1), 7 (2015).

176. Şahin, B., Aygün, A., Gündüz, H., Şahin, K., Demir, E., Akocak, S., and Şen, F., "Cytotoxic effects of platinum nanoparticles obtained from pomegranate extract by the green synthesis method on the MCF-7 cell line", *Colloids and Surfaces B: Biointerfaces*, Vol.163, 119-124 (2018).
177. León-Buitimea, A., Garza-Cárdenas, C. R., Garza-Cervantes, J. A., Lerma-Escalera, J. A., and Morones-Ramírez, J. R., "The demand for new antibiotics: Antimicrobial peptides, nanoparticles, and combinatorial therapies as future strategies in antibacterial agent design", *Frontiers in Microbiology*, Vol. 11, 1-8 (2020)
178. Ruiz, A. L., Garcia, C. B., Gallón, S. N., and Webster, T. J., "Novel silver-platinum nanoparticles for anticancer and antimicrobial applications", *International Journal of Nanomedicine*, Vol.15, 170-176 (2020).
179. Gopal, J., Hasan, N., Manikandan, M., and Wu, H. F., "Bacterial toxicity/compatibility of platinum nanospheres, nanocuboids and nanoflowers", *Scientific Reports*, Vol. 3(1) 2 -9 (2013).
180. Kumar, P. V., Kala, S. M. J., and Prakash, K. S., "Green synthesis derived Pt-nanoparticles using *xanthium strumarium* leaf extract and their biological studies", *Journal of Environmental Chemical Engineering*, Vol. 7(3), 103146 (2019).

الخالصة

تقنية النانو الخضراء هي تقنية جديدة أحدثت ثورة في مجال تصنيع المواد النانوية ذات الخصائص واألحجام واألشكال المميزة التي تكون كفاءتها موازية أو أفضل من المواد المحضرة بالطرق التقليدية وألهمية المواد النانوية في العديد من المجاالت ، بما في ذلك المجال الطبي. تم استخدام هذه الطريقة إلنتاج مركبات لها

خصائص عالجية آمنة ولها آثار جانبية قليلة باإلضافة إلى فعاليتها العالية.

يعد إنتاج الجسيمات النانوية المعدنية)MNPs(التي لها نشاط مضاد للميكروبات طريقة إضافية لمكافحة العدوى التي تسببها البكتيريا المقاومة للمضادات الحيوية.

حضرت جسيمات البالتين النانوية)PtNPs(باستخدام الطريقة الخضراء من مستخلص تمر الزهدي والخستاوي. حيث تم اختزال أمالح البالتين إلى جسيمات البالتين النانوية بنجاح في وجود المستخلص المائي للتمور الذي يعتبر مصد ًرا غنيًا للمواد الكيميائية النباتية التي أدت إلى اختزال Pt^{+4} إلى Pt^{0} من خالل توفير إلكترونات لهذه أأليونات.

تعتبر الطريقة الخضراء آمنة وسريعة وفعالة من حيث التكلفة مقارنة بالطرق الكيميائية والفيزيائية. حيث تظهر جسيمات البالتين النانوية كعوامل نانوية سامة ضد خاليا سرطان المبيض وسرطان المريء النشطة بيولوجيًا. أيضا اظهرت جسيمات البالتين النانوية كفاءة في تثبيط نمو بكتيريا *Pseudomonas aeruginosa* و *Streptococcus pyogenes*.

استخدمت التقنيات الفيزيائية لتشخيص جسيمات البالتين النانوية حيث أظهرت أألطياف المرئية لألشعة فوق البنفسجية حزمة رنين البالزمون السطحية)SPR(عند حوالي 283 نانومتر وأظهر طيف امتصاص أألشعة تحت الحمراء قم ًما مختلفة تتراوح من)400-4000(سم$^{-1}$ لتحديد المجموعات الوظيفية المسؤولة عن اختزال PtNPs. وتحليل المجهر اإللكتروني النافذ)TEM(أظهر أن PtNPs ذات شكل كروي . وعند الفحص بواسطة مجهر القوة الذرية)AFM(تبين تكوين جسيمات نانوية بقطر يتراوح من)30-40(نانومتر. واظهرت صور المجهر اإللكتروني الماسح)SEM(ان الجسيمات النانوية ضمن النطاق الفعال للمواد النانوية من)1-100(نانومتر و فحص حيود أألشعة السينية (XRD) أي ضابين تكون جسيمات البالتين النانوية عن طريق المقارنة بالطيف القياسي الخاص بإنتاج جسيمات البالتين على شكل بلورات نانوية.

تم تعريض الخاليا السرطانية التي تشمل خط خاليا سرطان المبيض SKO-3 وخط خاليا سرطان المريء SK-GT-4 لسلسلة من تراكيز جسيمات البالتين النانوية المحضرة)0.00125 ، 0.0025 ، 0.005 ، 0.01(موالري وتم قياس معدل تثبيط النمو في الخاليا بعد 72 ساعة. أظهر فحص السمية الخلوية أن هناك تأثي ًرا شديد السمية على الخاليا السرطانية كما وتم تعريض بكتيريا *Pseudomonas aeruginosa* و

Streptococcus pyogenes لسلسلة من تراكيز جسيمات البالتين النانوية المحضرة)0.00125 ، 0.0025 ، 0.005 ، 0.01(موالري . وأظهرت النتائج فعالية تثبيط معنوية ومعدل تثبيط نمو البكتيريا يزداد مع زيادة التركيز.

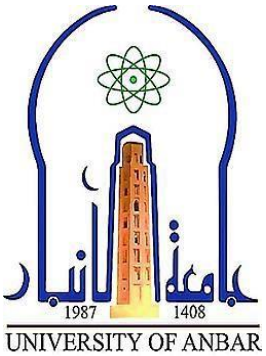
يمكن أن نستنتج من هذه الدراسة أن جسيمات البالتين النانوية المحضرة أعطت نتائج أولية جيدة ومشجعة للعمل المستقبلي كعامل مضاد للسرطان ومضاد للميكروبات.

و ازرة التعليم العالي والبحث العلمي

جامعة ألنبار

كلية العلوم قسم

الكيمياء



تحضير وتشخيص جسيمات البالتين النانوية باستخدام مستخلص التمور الع ارقية ود ارسة تطبيقاتها الطبية

رسالة

مقدمة إلى كلية العلوم - جامعة ألنبار

وهي جزء من متطلبات نيل شهادة الماجستير في علوم الكيمياء

من قبل الطالبة

نسرين حسن علي الجميلي

بكالوريوس كيمياء 2002 م

بأش راف

أ . د . أحمد مشعل محمد

جامعة ألنبار - كلية العلوم

1442 هـ 2021 م