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Theme

Design, Synthesis and Characterization of a New Ecological Bio-nanocomposite and Study of its Application

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Dedications

And we did not embark on the beginning except by His facilitation, and we did not reach the end except by His success.

So praise be to Allah who granted me success to reach this step in my academic journey.

I dedicate the fruit of my success to the one who eased hardships for me with her prayers ***''my mother''***

and to ***''my father ''*** *may Allah have mercy on him and reunite me with him in the gardens of bliss — may his resting place be blessed.*

And to my brothers, ***Ali*** *and* ***Hamza****, who were a support throughout this academic journey.*

And to my sister ***Naziha*** *and her two daughters,* ***Roumaissa*** *and* ***Sujoud.***

To my fiancé ***Bilal*** *O Allah, bless him for me and place between us affection and mercy.*

And to my friend ***Imane****, who was a companion throughout my academic journey and a partner in completing this work.*

Now I have completed the first steps of success by His grace, Glorified and Exalted Be He.

Razika

Dedications

In the name of Allah, the Most Gracious, the Most Merciful,

Peace and blessings be upon our Prophet Muhammad, the noblest of messengers.

To begin,

I open this dedication with praise and gratitude to Allah—my Lord, my helper, and my unwavering support. To Him belong all thanks and appreciation for as long as I live.

To my dear parents, who gave their effort and endured hardship, accompanying me with prayers and support throughout every stage of my education—

Thank you, ***my mother****. Thank you,* ***my father****.*

To my siblings: ***Abdelrahman, Salma****, and* ***Abdelnour,***

And to all my family members, especially my beloved grandmother—may Allah prolong her life.

To my friend, sister, and partner in this work, ***Razika,*** *companion in ambition and perseverance.*

To my dear friend Hajer, a true companion on this journey.

To Gaza, the enduring symbol of resilience and dignity — I dedicate this work as a humble tribute of loyalty and unwavering hope.

Imane

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Abstract

This study aims to develop therapeutic nanostructured systems using nanotechnology and an environmentally friendly approach that utilizes medicinal plants for nanoparticle synthesis. Green synthesis of nanoparticles was performed using *Rumex vesicarius* extract, selected for its well-documented antioxidant and anticancer properties.

In the first application, drug delivery carriers were fabricated using alginate polymer combined with silver nanoparticles (Ag NPs) and zinc oxide nanoparticles (ZnO NPs), and were loaded with bioactive substances exhibiting antioxidant, antibiotic, and anticancer properties. The resulting microspheres were designed for sustained release and incorporated different active ingredients, including mastic oil, vitamin C, and vitamin B12. In the second application, nanostructured therapeutic dressings were developed to enhance burn healing and wound closure. This involved the use of Haloxylon spp., a plant known for its regenerative properties and ability to stimulate skin cell proliferation. Silver and zinc oxide nanoparticles synthesized from this plant were embedded in an alginate polymer matrix, enriched with mastic oil to boost its healing efficacy. Physicochemical characterization of the synthesized materials was conducted using scanning electron microscopy (SEM), X-ray diffraction (XRD), and UV–visible spectroscopy. UV–Vis analysis confirmed the formation of silver nanoparticles using *Rumex* extract. XRD and SEM results demonstrated the crystallinity, morphology, and nanoscale dimensions of the ZnO and Ag nanoparticles, along with successful loading of the active compounds.

The release behavior of the microspheres was evaluated in reconstituted media at pH 7.4 (simulating colonic conditions), and antioxidant activity was assessed using the DPPH assay. Results showed that the plant extracts and their corresponding nanoparticles exhibited strong antioxidant activity, which enhanced the performance of the drug delivery beads. Optimal release of mastic oil, vitamin C, and vitamin B12 was observed at pH 7.4. These carriers function as smart systems capable of targeted and sustained drug release. Overall, the eco-friendly nanoparticles synthesized from medicinal plants demonstrated enhanced therapeutic efficacy and supporting their potential use in both drug delivery systems and wound healing. Moreover, mastic oil/ZnO nanoparticle-loaded beads showed effective controlled release of active compounds and are particularly promising for colon cancer treatment.

Keywords: Alginate polymer, zinc nanoparticles, silver nanoparticles, green synthesis, drug carriers delivery, dressings.

Résumé.

Cette étude vise à développer des systèmes thérapeutiques nanostructurés en utilisant la nanotechnologie et une approche respectueuse de l'environnement reposant sur l'utilisation de plantes médicinales pour la synthèse de nanoparticules. La synthèse verte des nanoparticules a été réalisée à l'aide de l'extrait de *Rumex vesicarius*, sélectionné pour ses propriétés antioxydantes et anticancéreuses bien documentées.

Dans une première application, des vecteurs de délivrance de médicaments ont été fabriqués à partir d'un polymère d'alginate combiné à des nanoparticules d'argent (Ag NPs) et d'oxyde de zinc (ZnO NPs). Ces vecteurs ont été chargés en substances bioactives présentant des propriétés antioxydantes, antibiotiques et anticancéreuses. Les microsphères obtenues ont été conçues pour une libération prolongée et ont incorporé différents principes actifs, notamment l'huile de mastique, la vitamine C et la vitamine B12. Dans une seconde application, des pansements thérapeutiques nanostructurés ont été développés pour favoriser la cicatrisation des brûlures et la fermeture des plaies. Cela a impliqué l'utilisation de *Haloxylon* spp., une plante connue pour ses propriétés régénératrices et sa capacité à stimuler la prolifération des cellules cutanées. Les nanoparticules d'argent et d'oxyde de zinc synthétisées à partir de cette plante ont été intégrées dans une matrice polymérique d'alginate enrichie en huile de mastique pour renforcer son efficacité curative.

La caractérisation physico-chimique des matériaux synthétisés a été réalisée par microscopie électronique à balayage (MEB), diffraction des rayons X (DRX) et spectroscopie UV-visible. L'analyse UV-Vis a confirmé la formation des nanoparticules d'argent à partir de l'extrait de Rumex. Les résultats de la DRX et de la MEB ont mis en évidence la cristallinité, la morphologie et les dimensions nanométriques des nanoparticules de ZnO et Ag, ainsi que le bon chargement des composés actifs.

Le comportement de libération des microsphères a été évalué dans un milieu reconstitué à pH 7,4 (simulant les conditions du côlon), et l'activité antioxydante a été mesurée à l'aide du test DPPH. Les résultats ont montré que les extraits de plantes et leurs nanoparticules associées possédaient une forte activité antioxydante, ce qui a amélioré la performance des billes de libération de médicament. Une libération optimale de l'huile de mastique, de la vitamine C et de la vitamine B12 a été observée à pH 7,4.

Ces vecteurs fonctionnent comme des systèmes intelligents capables d'une libération ciblée et prolongée des médicaments. Globalement, les nanoparticules écologiques synthétisées à partir de plantes médicinales ont démontré une efficacité thérapeutique améliorée, soutenant leur utilisation potentielle dans les systèmes de délivrance de médicaments et dans la cicatrisation des plaies. De

plus, les billes chargées en huile de mastique et en ZnO ont montré une libération contrôlée efficace des composés actifs et sont particulièrement prometteuses pour le traitement du cancer du côlon.

Mots-clés : Polymère d'alginate, nanoparticules de zinc, nanoparticules d'argent, synthèse verte, vecteurs de médicaments, pansements.

الملخص:

تهدف هذه الدراسة إلى تطوير أنظمة علاجية نانوية باستخدام تكنولوجيا النانو ومنهجية صديقة للبيئة تعتمد على استخدام النباتات الطبية لتصنيع الجسيمات النانوية. تم إجراء التخليق الأخضر للجسيمات النانوية باستخدام مستخلص نبات*Rumex vesicarius* ، الذي تم اختياره لما له من خصائص مضادة للأكسدة ومضادة للسرطان موثقة جيدًا.

في التطبيق الأول، تم تصنيع نواقل دوائية باستخدام بوليمر الألجينات مدمج مع جسيمات نانوية من الفضة (Ag NPs) وأكسيد الزنك(ZnO NPs) ، وتم تحميلها بمواد نشطة حيويًا ذات خصائص مضادة للأكسدة، ومضادة للبكتيريا، ومضادة للسرطان. صُممت الكريات المجهرية الناتجة لتحرير مستدام واحتوت على مكونات فعالة مثل زيت المصطكى، فيتامينC ، وفيتامينB12

في التطبيق الثاني، تم تطوير ضمادات نانوية علاجية لتحفيز التئام الحروق وإغلاق الجروح. تم استخدام نبات .*Haloxylon* spp المعروف بخصائصه التجديدية وقدرته على تحفيز تكاثر خلايا الجلد. تم دمج جسيمات الفضة والزنك النانوية المستخلصة من هذا النبات في مصفوفة بوليمر الألجينات، المعززة بزيت المصطكى لتحسين فعاليتها العلاجية.

تمت دراسة الخصائص الفيزيائية والكيميائية للمواد المُصنّعة باستخدام المجهر الإلكتروني الماسح(SEM) ، حيود الأشعة السينية (XRD)، والتحليل الطيفي بالأشعة فوق البنفسجية .(UV–Vis) أكدت تحاليل UV–Vis تكوين الجسيمات النانوية الفضية باستخدام مستخلص .Rumex وأظهرت نتائج XRD وSEM بلورية وشكل وحجم الجسيمات النانوية من ZnO وAg، بالإضافة إلى نجاح تحميل المركبات النشطة.

تم تقييم سلوك إطلاق الكريات المجهرية في وسط محاكى لظروف القولون عندpH 7.4 ، وتم اختبار النشاط المضاد للأكسدة باستخدام اختبارDPPH . أظهرت النتائج أن المستخلصات النباتية وجسيماتها النانوية تتمتع بنشاط قوي كمضادات أكسدة، مما يعزز من كفاءة حبيبات التوصيل الدوائي. وقد تم تسجيل إطلاق مثالي لزيت الضرو، فيتامينC ، وفيتامين B12 عندpH = 7.4

تعمل هذه الحوامل كنظم ذكية قادرة على التحرير المستهدف والمستدام للدواء. بشكل عام، أظهرت الجسيمات النانوية الصديقة للبيئة المُحضرة من النباتات الطبية فعالية علاجية محسّنة، مما يدعم استخدامها في أنظمة توصيل الدواء وكذلك في شفاء الجروح. علاوة على ذلك، فإن الحبيبات المحملة بزيت الضرو و أظهرت إطلاقًا فعالًا ومحكومًا للمركبات النشطة، وهي واعدة بشكل خاص لعلاج سرطان القولون.

الكلمات الرئيسية: بولمير لالجينات ، جسيمات الزنك النانوية , جسيمات لفضة النانوية ، طريقة الخضراء ، ناقلات لادوية ، ضمادات.

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Chapter I: Bibliographic Study

Chapter II: Experimental Method

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List of abbreviations

NPS: nanoparticles

Ag NPs: silver nanoparticles

ZnO NPs: zinc oxide nanoparticles (**Zinc acetete**)

SEM: Scanning electron microscopy

EDS: Energy – dispersive X- ray spectroscopy

UV-visible: Ultraviolet – visible spectroscopy

FTIR: Fourier transform infrared spectroscopy

TEM: Transmission electron microscopy

XRD: X – ray diffraction

hBN: Hexagonal - born nitride

MX2: Metal dichalogenides

CNTs : Carbon nanotubes

MMNC : Metal matrix nanocomposites

PMNC : Polymer matrix nanocomposites

CMNC: Ceramic matrix nanocomposites

FETS: Field – effecte transistors

DCS: Differential scanning calorimetry

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General Introduction

Since the emergence of the term "nanotechnology" the world has witnessed remarkable development across various fields, including medicine, electronics, food and energy **[1]**, among these, the medical field stands out as one of its most significant applications. Nanotechnology has contributed to the advancement of medical equipment, such as drug delivery systems, biosensors and medical imaging devices used in diagnostics **[2].** These advancements rely on materials at the nanoscale typically ranging between 1 and 100 nm **[3].** Nanomaterials possess unique chemical and physical properties that distinguish them from their bulk counterparts, particularly Nanoparticles, wich are characterized by a high surface area. This feature grants them high efficiency and performance, making then suitable for use in both diagnosis and therapy – especially in the treatment of chronic and complex diseases such as diabetes, cancer, as well as in the healing of burns and wounds.

Based on this back ground, the present dissertation aims to highlight the importance of harnessing the unique properties of nanomaterials to develop effective therapeutic solutions, this work falls within the scope of research on nanomaterials and their applications in designing drug delivery systems, specifically engineered to combat cancer, with a particular focus on targeting colon cancer cells, given their significant relevance in the medical field, these nanomaterials were also utilized in the development of therapeutic dressings designed for the treatment of burns and wounds.

Biologically active materials were employed through the use of a green synthesis approach, wich focuses on the fabrication of nanomaterials derived from natural sources such as plants. additionally, a polymeric material was utilized to synthesized polymer – based nanoparticles, in order to exploit their potential in the design of drug delivery systems and therapeutic dressings. This offers promising application in the medical field and constituted the main objective and contribution of this thesis.

The methodology of this thesis is comprehensive, as it combines both theoretical study and laboratory preparation, thereby granting it a practical and theoretical character that reflects modern approaches in the development and design of therapeutic solution based on nanotechnology.

This master's thesis is divided into several chapters, the first chapter presents a theoretical background on the concept of nanotechnology, nanomaterials, their synthesis methods and the different type they encompass. It also highlights their properties and various applications. Additionally, the theoretical section addresses the understanding of drug delivery systems.

Another chapter of this thesis is dedicated to the practical implementation of the research idea – mainly, the experimental chapter. In this section, we provided a detailed explanation of the step involved in the fabrication of both the anticancer drug delivery systems targeted at colon cancer and

the therapeutic wound and burn dressings. Undoubtedly, the synthesized materials required thorough characterization, therefore, a subsequent chapter was devoted to the methods and tools used for the characterization of these formulations. The results obtained from these analyses were then presented in the final and most crucial chapter, which aimed to elucidate the mechanisms and properties of the anticancer drug carriers and the therapeutic dressings.

Chapter I:

Bibliographic Study

I.Nanotechnology:

The nanotechnology this term was coined in 1974 by Norio tamiguche **[4]** to specializes in the study, measurement and manufacture of materials, atoms and molecules at the nanoscale **[5],** which the materials in the size range of [1- 100] nm **[1]** or size of a billionth of a meter.

In nanotechnology materials with distinctive properties are generated due to the size of the materials, which are given special chemical, physical and biological properties **[6]** these properties of nanomaterials differ from those of individual, bulk materials **[7]** nanotechnology depends on converting both atoms and molecules into new shapes in order to produce materials with high-percision properties and performance **[8].**

Nanotechnology that work by tow techniques to providing materials at nanoscale this technique is: top-down and bottom up. nanotechnology has been introduced in many fields where it has become prominent in many applications.

The application of nanotechnology appeared in medical aspect, electronics, energy and food …. **[1].**

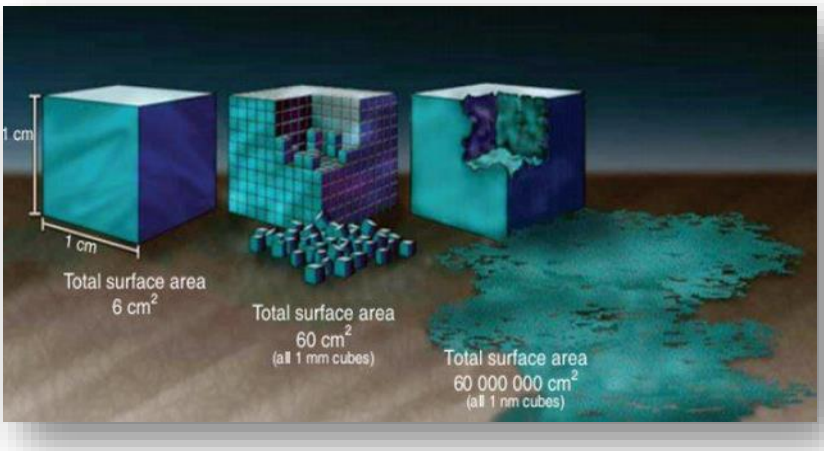


Fig I.1. effect of size reduction on the increase of surface area in nanomaterials

I.1. Nanomaterials:

I.1.1. Definition:

Nanomaterial it is a type of material that has a nanoscale size, this is less in dimension **[9]** or order of a billionth of a meter 10^{-9}.

Nanomaterials have nanostructure this structure it is created via to processes can be chemical processes and thermal processes and physical processes **[1]** therefore nanomaterial is not limited to determining the size of an atom or molecule, but rather provides a decryption of geometric sizes **[10].**

The size of nanomaterials is responsible for determining their properties **[9],** the optical, magnetic, electrical and mechanical properties make the nanomaterials more effective, unique and efficiency **[11]** this efficiency is demonstrated through the large surface are to volume ratio.

I.1.2. Types of nanomaterials:

Nanomaterials have many types, these types are classified according to their dimonenality that have 0D, 1D ,2D and3D materials **[12],** also can be classified according to their composition we find that nanomaterials are divided into types due to the components that they are formed from, carbon-based materials, inorganic-based, organic-based and composite nanomaterials **[13].** It have according to morphology **[12],** to the pore size and to the the origin of nanomaterials**[14].**

I.2.2.1. Classification of nanomaterials according to the origin :

The origin of nanomaterials is diverse and different; this basis we can classify nanomaterials based on their origin.

Nanomaterials can be classified natural , incidental, engineered nanomaterials **[13]:**

a. Natural nanomaterials:

They are materials produced in nature without any industrial processes. By geological, mechanical or biological methode **[15]** since the sources of nanomaterials are multiple in nature, among them:

Forest fires, ocean, spray, volcanic ask, mineral remains of eroded rocks **[15],** and photochemical reaction **[16]** where it is found in living organisms including plants, animals and humans.

It is also found in bacteria algae and viruses **[13].** This natural nanomaterials can be organic or inorganic materials, it can also, be produced by human activates **[17].**

b. Engineerd nanomaterials:

They are material that are manufactured by chemical, physical or hybrid methodes **[16]** this methode include chemical manufacturing, welding and crude refining **act [13].**

Depending on the dimensionality and their characterizatics where have spheres, rings and tub shapes **[15]** that have high surface area and strain, crystallographically controlled aggregation unsual phase transformation **[17],** the nanoscales metal oxides it one of engineered nanomaterial metal oxides it one of nanocages, where used in drug delivery and as sensor dvices **[13].** Other engineered nanomaterials like nanocarbon, metalloids, homopolymers, copolymers, organic and inorganic nanomaterials and self-assembled **[18].** The homogenous composition, high reproducibility and narrow size is a factors which indicates consistency and quality of engineered nanomaterials **[18].**

c. Incidental nanomaterials:

It is be found in atmosphere, surface and marine water and soils, they are by-products of chemical processes **[13]** and of human activate , so that the size and shape of these materials cannot be controlled **[15]**one of the most prominent incidental materials is cosmic dusts it contains in its components, nitride, silicate, carbon, carbide and nanomaterials with organic compound **[13]** these materials are produced by human activates like vehicle exhaust gases, combustion drug coming and welding gases **[15]** incidental nanomaterials are used in trains ships aircraft and in natural processes act **[16]**.

I.2.2.2. Classification of nanomaterials according to dimensions:

Nanomaterials according to their dimension or size that have zero-dimension, one-dimension, tow dimension and three dimension **[12].**

a. Zero dimensions (0D) Nanomaterials:

In these type of nanomaterial there is no micro-dimension, fined all three dimension at Nanoscale **[14]** is found in polymer dots, quantum dots, carbon quantum dots, fullerene **[19]** (0D) have crystalline or amorphous texture **[14]** the structure of zero dimension are spherical or quasi- spherical that have a large -surface area and quantum confinement effect **[19].**

Fig I.2. Zero-Dimensional materials (a)-Fullerene C60 and (b)- Carbon Dots

b. One dimensions (1D) Nanomaterials:

One of its dimension exceeds the range of the nanoscale **[14]** has a characteristic crystalline or amorphous, can mono-crystallite or multi-crystalline materials**[13]** contains all of : Nanowire, metabolic, Nanotube, polymeric, Nanorodes, filament or fiber **[12]** where the one dimensions materials contributed to several uses like electronic systems and transparent conductors **[20].**general Nano structure play a role in electrochemical energy storage and rechargeable batteries **[21]** .one dimensions that have a electrical, thermal, mechanical properties **[22]** .

(a) *(b)*

Fig I.3. one-dimensional (1D) materials (a)- MWNT and (b)-SWNT

c. two dimension 2D Nanomaterials:

This materials have two non-Nano dimensions , it is amorphous or crystalline materials, where it is in the form of thin films , mono - layered and multi – layered Nanoplates **[12]** coatings , Nanosheets free particle tubes , fibers and ultra-fin **[14]** it is also one of thinnest nanomaterials due to the thin thickness of which it is composed, it consists if Strong bonds wich forms a layered structure where it is present inside this layer forces of van der Waals (it is a weak forces) **[13]** two dimension nanomaterials include Graphene hexagonal boron nitride (hBN) and metal dichalcogenides (MX_2) **[13]** these materials characterized by high surface area and quantum -size effect which makes it has physiochemical properties **[23]** and solar cells, catalysts, batteries (lithium)and electronics **[24]** it can also be used as Nanofillers this is in the heat transfer fluids, due to their high surface area ,this surface Works effectively in transferring heat **[25].**

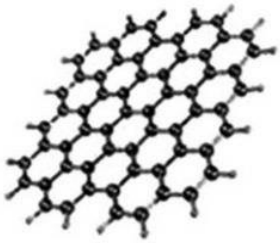


Fig I.4. two-dimensional (2D)- materials – Graphene-

d. Three-dimension 3D Nanomaterials:

Are a materials with all three dimension exceeds the range of the Nanoscale (big ger than 100nm) **[12]** or what is called bulk materials **[14]** these materials may be represented by fibers polocrosse's, carbon nanobuds, nanotubes pillars, larges skeletons **[12]** bundles of nanowires and nanotubes , thin films with atomic – scale ,colloids **[14].**

Three dimension material characterized by complex structure due to the surface if the material, which is designed using high technologies **[26]** . three dimension nanomaterials include the dispersions of nanoparticles the latter is multi – layered **[13].**

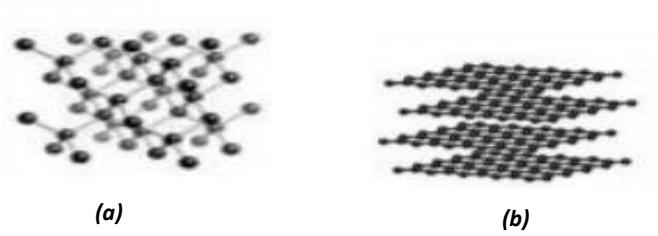


Fig I.5. three-dimensional (2D) materials (a)-Diamond ,(b)- Graphite

I.2.2.3. Classification of nanomaterials according to composition:

Nanomaterials can be classified into groups, where these classifications are based on the materials they are composed of. There is organic – based, carbon – based, inorganic – based and nanocomposite **[14].**

a. Carbon – based Nanomaterials:

They are nanomaterials that mainly composed of carbon this carbon present in diamond and graphite, carbon – based materials can be in form of hollow tubes, spheres, ellipsoids **[12]**, nanowires, Nanoparticules , layer.

That include carbon nanofibers, fullerenes (C60), graphene, carbon black, carbon nanotubes (CNTs) **[13].** the properties of carbon, where among the manufacturing methodes the laser ablation, chemical vapor disposition (CVD) and arc discharge **[12].**

These materials are known to have great strength and are used to strengthen structures **[14]** carbon – based nanomaterials characterized by small size, high- surface area, thermal conductivity , high electrical mechanical and optical properties **[27]** and have high purity and functions present on the surface of the materials, wich made it also used as means of delivering pharmaceutical preparation **[28].**

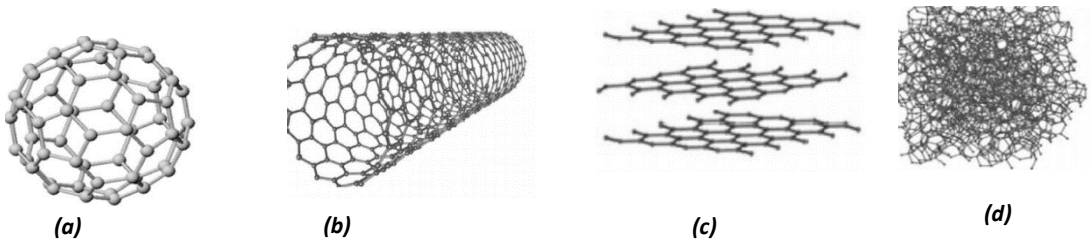


Fig I.6. Carbone based materials (a)- Fullerene C60, (b)- Singl_Walled carbon nanotube,(c)- Graphite, (d)- Amorphe carbone [11].

b. Organic - based Nanomaterials:

Is nanomaterials made of organic materials where it is formed by covalent interaction **[13].** Dendrimers, micelles, polymer and liposomes these are categories of organic nanomaterials **[12]** can

be to form nanospheres or nanocapsule or hollow sphere, they are also naturally biodegradable materials that used to deliver medication **[28]** where we find for each categories a specific property and uses.

So the micelles and liposomes are biodegradable and non- toxic this allows then to be used in pharmaceutical transportation **[28]** and dendrimers are used as a Nanosensor, due to the holes it contains in its structure, it can also be used as a drug delivery **[14].**

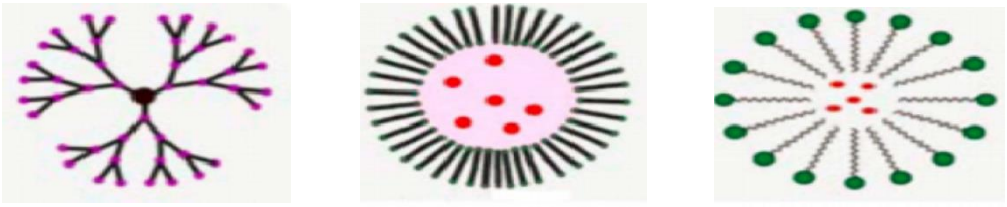


Fig II.7. Materials with organic compounds (a)- Dendrimer, (b)- Liposome, (c)-Micelle [28].

c. Inorganic – based Nanomaterials:

They are non-carbon nanomaterials composed of inorganic materials **[14]** where these materials are metals, metal oxides **[12]** inorganic nanomaterials include the metallic, metal oxide, semiconductor, ceramic Nanomaterials. This is due to its components.

Gold nanoparticles, magnetic nanoparticles, nonporous they are among the most prominent inorganic nanomaterials, it also widely used in the medical field. for example, in bioimaging and radiology and drug delivery especially in cancer therapies rich has witnessed a great recovery **[29]** and among the most important the magnetic nanomaterials this is due to its magnetic properties **[28].**

Inorganic nanomaterials are manufactured in the form of vesicles Nanocarriers for the pharmaceutical, in order to deliver medicines to the targeted locations **[30].**

- **Metal – based Nanomaterials :**

It is mainly composed of metal, thes metal are: Aluminum (Al), cobalt (Co), cooper (Cu), iron(Fe), silver (Ag), zinc (Zn), lead (Pb) **[31],** it is the basic minerals used to syntheses the metal nanoparticle. through the constructive or destructure processes, the metal nanomaterials are synthesis **[14]** to give a nanomaterial with high surface area to volume ratio, ore size, crystalline structure, color and spherical **[31]** that have a electrical, catalytic, thermal and optelectrical **[12,28].**

Metal nanomaterials especially noble metal nanoparticles had wide use in the medicine, where has been used in treating cancer and eliminating germs and funge, in addition to being used as carrier of drugs and genes **[28].**

- **Metal oxide Nanomaterial:**

Contains in its composition on metal and oxygen to give metal oxide in nanoscale reng.

Synthesis of nanoparticles of metal oxides gives then properties and efficiency **[31].** metal oxide nanomaterials include zinc oxide (ZnO), silicon dioxide (SiO_4), aluminum oxide (Al_2O_2) , titanium oxide (TiO_2) **[14]** , this materials has been used in many applications and among its most important application are in medicine , electronics , energy, environment , catalysis , biomedical **[32].**

Furthermore, it was used as a gas sensor and anode for fuel cell **[33]** these application are due to chemical, electronic , magnetic properties of metal oxide nanomaterials **[32]** where find that these properties are related the size and shape of metal oxide nanomaterials **[33]** these materials has a wide share in the field of medicine , especially biomedicine , in addition it is antibacterial materials **[28]** it is considered one of the most effective against bacteria .

- **Semiconductor – Nanomaterials:**

It is a class of materials that has the properties of insulator and conductor **[34]** that have electronic, optical, chemical and physical properties. due to this properties, it has many features including the continuous absorption bands, high chemical, narrow and intensive emission spectra ect **[35,36]** the quantum confinement effect is one of the most prominent features of semiconductor as it controls the optical . properties **[36]** the surface area, surface to volume ratio and quantum confinement effect related to size change **[35].**

Semiconductor nanomaterials contains the following type **[34]:**

- Elemental semiconductors
- Binary compounds semiconductor
- Tenary alloy semiconductor
- Quaternery alloys semiconductor

The methodes of synthese the semiconductor nanomaterial includes, laser ablation, carbon nanotube template methode, molten salt methode, solution – liquid – solid (SLS) methode and template electrochemical methode **[37].**

- **Ceramic nanomaterials:**

Ceramic nanomaterials are inorganic metalloid solid, using oxides, carbides, carbanates and phosphates by heating, cooling and this is in succession **[38]** can be with crystalline, hollow or porous, amorphous structure **[28].**

Ceramic nanomaterials have many properties like electrooptical, superconductive, ferroelectric, ferromagnetic, high affinity and antimicrobial **[12,38].** Through these properties, it has applications in photo – degradation, catalysis **[31]** and in drug delivery to eliminate some tumors and germs **[14]** it also known to be anti-caries and his contribution to the PH adjustment wich promotes dental health **[38].**

d. Nanocomposites:

They are composite materials that contain at least two phases in their composition, one of which is at the nanoscale **[39].** Nanocomposite include according to the matrix materials which contains: metal matrix (MMNC), polymer matrix(PMNC) and ceramic matrix nanocomposites (CMNC) **[7]** it has properties makes different from the bulk materials and represented in large surface area, small size, the interactions with the matrix and are high performance materials **[40,39].**

The Nanosized reinforcement these are the components that the matrix contains, where it is in a form fiber, nanotube, whiskers or particles **[41].**

e. According to morphology:

Nanomaterials can be classified based on what called morphology, wich concerned with shape, size and structure **[42]** the morphology of nanomaterials determination depends on the flatness, aspect ratio, sphericity and spatial position **[12,13]** different forms of nanomaterials have physical and chemical properties, this properties determined by the shape **[42],** where nanomaterials are classified as **[43,13]:**

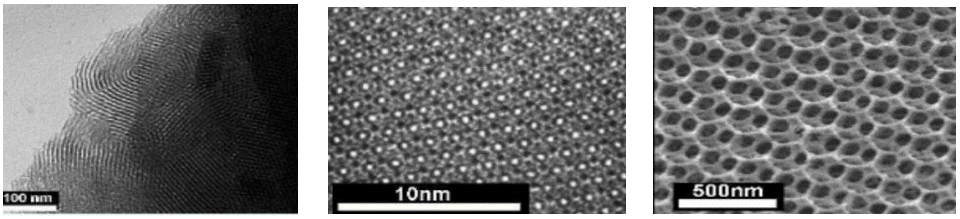
- Materials with high aspect ratio : They include Nanowires, Nanotube, Nanobelts, Nanozigzags, Nanopillers and Nanohelices.
- Materials with low aspect ratio: They include Nanopillars, Nanospherical, Nanohelices, Nanocubes, various, Nanopyramids and Nanowires

I.2.2.4. Classification of nanomaterials according to pore size :

The pore size varies in nanopours materials, this difference in size males nanopours divided into three type : microporous , mesoporous and macropours materials **[44]** the shapes of pores, the size distrubution and the diameter of the pore, they are factors that affect the properties and performances of nanopours and also on determines of the moleculs size **[11,14]**the pore size also determines the type and properties of the reaction.

Nanoporeus used in many application, it used in adsorption, energy, catalyses, sensing, purification, in medicine. Where have high surface area to volume ratio **[11].**

a. **Microporous materials :** Are materials with pore size between 0 and 2nm pores (less than 2nm) **[44].** These pores are narrow and characterized by high interaction and slow diffusion Kineties **[14].**
b. **Mesoporous materials :** The pore size in mesoporous materials in the range of 2nm to 5nm **[44]** of it formes, carbon mesoporous materials , MCM- 41, MCM-48 and SBA- 15 **[14].**
c. **Macroporous materials :** In this, the pore size is larger than 50 nm **[11]** it belongs to polyromantic or small biological molecules they include carbon microtube, pourous gels and glasses find application as matrices, xaffolds, catalytic and sensing **[14].**



Microporeuse Materials *Mesoporous Materials* *Macropours Materials*

Fig I.8.type of pore size in nanomaterials.

I.2.3. Syntheses methode of nanomaterials:

Nanomaterials are synthesized by two approaches:

Top – down and bottom – up **[45]** thes two approaches contain methodes where top – down include physical methode and in bottom – up fined biological and chemical methodes **[46]** the shape, type of application of nanomaterial, materials used, concentration of reacting materials, temperateur and PH all these controls and influences in the methode of synthesis nanomaterials **[46,47].**

I.2.3.1. Top – down approche :

It is one of the method of synthesize nanomaterials. It is relies on physical methods in its approach, where it depends on cutting the bulk materials into nanomaterials **[48]** this is done by applying the force of large materials and causing then to break up into nano-sized pieces **[49]** making it similar in its approach to semiconductor industry **[50].** This approach include laser ablation, mechanical milling, etching, sputtering, electro – explosion **[51],** lithographic methodes and high energy methode this approach is not suitable for sensitive materials **[49].**

Mechanical milling is the simplest top – down approach which enable the production of nanomaterials is grates abundance than other methode **[47]** and specifically high energy bulk milling through wich it is produced nanograins, nanocomposites, nano-quasicristallin and Nanoalloy **[52].**

I.2.3.2. Bottom – up approche:

It is a method that basically depends on assembling all atoms or molecules on nanoscale, that are in an individual form into structures with nano dimensions **[52]** using chemical and biological methods, molecular recognition and self – assembly **[49,53]** this approch deals with the complexe composition of molecular or multi – component materials [50]it works by assembling all complex structures in the form of layers **[53].** This approach enables the production of nanostructured devices and materials with multiple functions, bottom up approach include sol – gel methode, atomic layer deposition, molecular self-assembly **[54],** chemical vapor deposition, electrodeposition and liquid phase methods **[47]** and green syntheses methode, the following diagram illustrates the mechanisem of the approche.

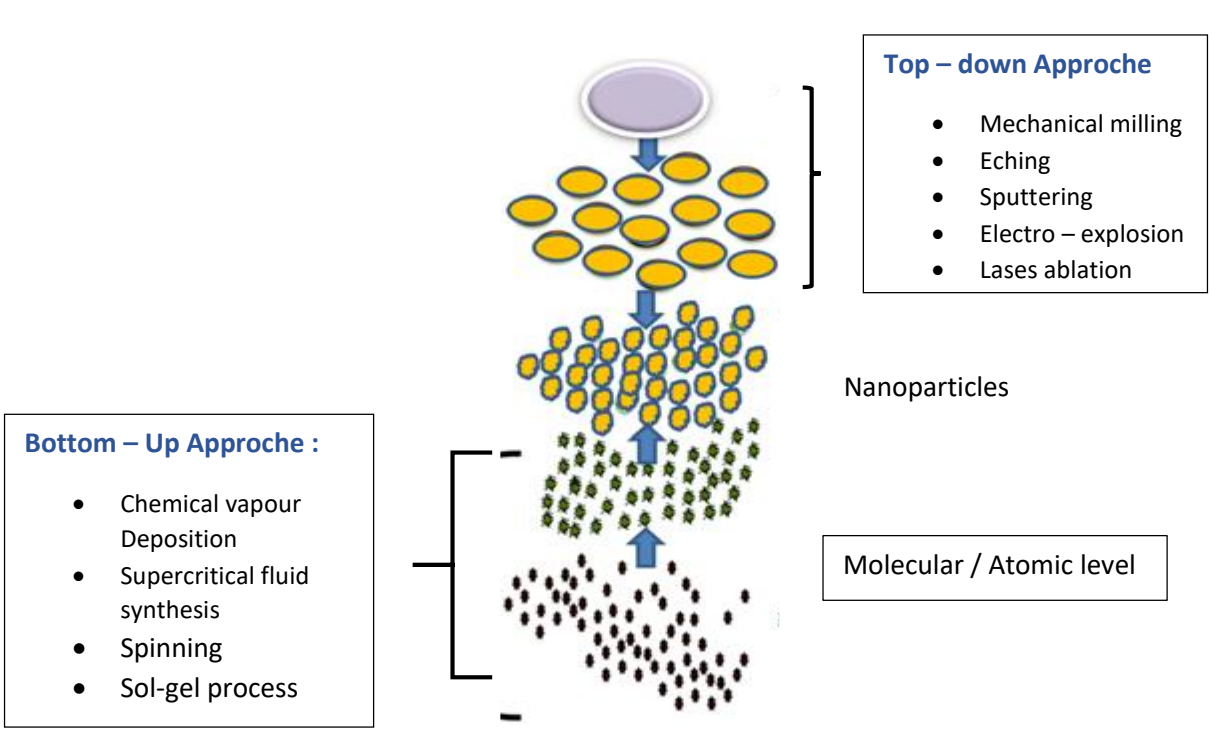


Fig I.9. methode Synthesis of nanomaterials.

I.4. Properties of nanomaterials:

I.4.1. Chemical properties:

Nanomaterials are distinguished from bulk materials by a special electronic structure and number of atoms that make up their surface. This is what makes nanomaterials distinguished by chemical properties that include reactivity and catalysis **[55].** Materials that have high surface energy are more reactive and active, which causes the instability of these materials, making then involved in many reactions **[56],** it was also found that nanoparticles with different shapes are used as catalysts **[57]** this is due to the high surface – to volume ration, which is one of the factors of catalytic property, is indirect relationship with it, as the higher this percentage the higher the catalytic property of nanomaterials **[56].**

I.4.2. Mechnical properties :

Nanomaterials have mechanical properties not found in bukl materials or even materials containing microparticles **[58]** thes prorperties include the ductility, elasticity, tensile strength and flexibility **[14].** Where these properties given many factor makes it different, these factors is hardness, strength, friction **[59],** toughness**[14].** Among the nanomaterials that have mechanical properties is the nanometelic materials where it has high hardness strength **[60].**

Mechanical properties of nanomaterials made it into many applications it is also used in modifying the surface of dvices and in nanofabrication processes **[58,60].**

I.4.3. Quantum confinement effect:

Spatial confinement and detention of electrons can occur and electron energy is confined to the electronic levels in a mobile and variable state in nanomaterials especially nanocrystalle materials, wich leads to the approach of the diameter and potential energy levels of the electron ti the DE Broglie wavelangth of the electrons. As a result, changes occur in energy levels, causing what is known as the quantum confinement effect **[61,62]** this phenomenon can be studied by controlling of the nanostructure and investigating the various effects that result from it **[63].** The quantum confinement effect is associated with the optical properties of nanomaterials, as well as various other properties such as electrical characteristics. This is because confinement contribates to the modification of the surface and crystal structures of nanomaterials **[61]** this phenomenon is

Observed in quantum dots composed of metals, semiconductors, as well as insulators and organic materials **[62].** This property can be observed using electron scaning microscopy (SEM).

I.4.4. High surface area- to volume ration:

Nanomaterials have high surface area to volume ration, which mean compared to its size and also inversely proportional to size **[55]** the surface area to volume ration is defined as relationship between the surface area of materials and its volum, where a decrease in volume leads to an increase in surface area particles or clusters with high surface area **[64]** per particle can be manufactured to obtain high surface areas for nanomaterials **[65]** this ration is fundamental property that makes the nanomaterials highly performing compared to the chemical reactivity increases, so that materials with a high surface area are characterized by high reactivity.

In addition able to determing the mechanical, electrical and optical properties, therefore, the surface area to volume ration is considered a tool that determines the behavior, reactivity and applications of nanomaterials **[64].**

I.5. Applications of Nanomaterials :

Table I.1. applications of nanotechnology in various fields.

The field	Materrials and applications
Catalyses	• Iron, silver, silica,aluminum and titanium dioxide **[66].** • Used as catalysis in :pharamaceutical fibers polymers, fine chemical, lubricants **[66]** and in some chemical reaction (reduction**)[67].**
Energy stroge	• Materials – based on platinum (Pt).Li- ion, Li-metal **[66].** • Used as supercapacitors, fuel celles, batteries, energy generation **[68]** for the purpose to storage, manufacturing improvements, energy saving and sources of energy **[67].**
Medicine	• Gold Nanomaterials (Au NPs), silver nanoparticles (Ag NPS), zinc oxide nanoparticles (ZnO), quantum dots **[66].** • Used as photothermal treatment, cancer treatment, biosensing, biolabing , photodynamic gene therapy **[66],** drug delivery, imaging, sensing and nanocarriers for chemotherapy **[69].**
Sensors	• Iron oxide, cadonium sulfited quantum dots, silver nanoparticles (Ag NPs), zinc oxide (ZnO NPs) **[66].** • Detection of pollutants, ensuring process safety in industries, healthcare monitoring **[70],** detection of staphyloccus aureus, liquefied petroleum gas sensors (LPG).
Environment	• Nickel oxide nanoparticles (NiO NPs) ,zinc oxide nanoparticles (ZnO NPs) **[59].** • Cleaning contaminated sites , environmental remediation **[68],** environmentally benign sustainable, products, sensor for environmental stage, removal of heavy metal **[59]** and water treatment .

Electronic	• CNTS, graphene, organic electronic molecule, metallic NPs, carbon – nanotube **[59,71]** . • Lattinger liquide behavoir, quantum wires and single electron transistors, ambipolaire FETS, ballistic transistors **[71],** solaire celles.

I.6. Nanocomposite materials:

I.6.1. Definition:

Central nanocomposite materials are combination of matrix and nano- dimensional particle, where the nanoparticle are distributed with in the matrix. These nanoparticles exhibit different chemical dimensions, contributing to the variation in properties of the nanocomposite materials **[72,73]** can also be described as multi- phase systems, where at least one of these phases dimensions at the nanoscale **[72]** the structural synergy enables the nanocomposite material to inherit the combined properties of its constituent materials, making it unique, these enhanced properties are not typically found in a single materials, these properties includes the mechanical strength, improved thermal stability, improved barrier properties, flexibility, electrical properties and optical transparency **[39]** its properties are depend on degree of thermos, degree of polymer, polymer chain mobility, polymer chain conformation **[72]** the interfacial interactions and the environmental conditions.

Due to these unique properties nanocomposite materials have found widespread applications particularly in pharmaceutical (drug delivery) , biomedical materials, catalysis **[40],** food and agriculture, electronics and information technology , environment remediation **[74]** and optical, biological application this materials where in form fiber, nanotube, whiskers or particles **[41]** are represented in large surface area, small size, the interaction with the matrix and high performance materials **[39,40].** Nanocomposites materials are synthesized using various methods including: in-situ polymerization technique, molten or melt intercalation technique **[74],** sol- gel methode, co-precipitation method.

Nanocomposite require a comprehensive characterization of all their aspects, wich is achieved using various techniques among the most prominent technique are: scanning and transmission electron (SEM and TEM), tunneling microscopy (STM), transformed infrared spectroscopy (XPS), differential scanning calorimetry (DCS) **[40],** X-ray diffraction(XRD) .

I.6.2. Classification of nanocomposites :

I.6.2.1. Metal matrix nanocomposite (MMNCs):

Metal matrix nanocmposites are materials that combine two distinct phases, each possessing different properties**[7]** these two phases consist of a metallic matrix and nanoparticles where the nanoparticles are incorporated and uniformly distributed with in the metallic matrix **[75]** nanoparticles exhibite unique mechanical, physical and chemical properties that are not present in metallic matrix, thereby enhancing its chemical and transforming it into a reinforced metal matrix nanocomposites **[72,76]** also it enhance the properties of the metallic matrix, improving its overall performance and functionality **[75]** therefore, the incorporated nanoparticles act as reingforcing agents for the alloy or metallic matrix, endowing these materials with a combination of properties such as hardness, elastic modulus and tensile strength, which are characteristic of both ceramics and metals **[7]** in addionally , mechanical, physical properties, thermal conductivity, fraction coefficient, wear resistance and low price etc**[76].** thes Materials are synthesized by either adding nanoparticles to the metal, a method known as situ methods, or by in situ synthesis of ceramic nanomaterials through a reaction during processing, the syntheses methodes can also be classified based on the phases of fabrication into liquid, solid and semi-solid processes **[75]** a faw examples for metal matrix nanocomposites are then aluminum matrix nanocomposite (Al MNCs),copper matrix nanocomposite (Cu MNCs) and magnesium matrix nanocomposite (Mg MNCs)**[76].**these materials are now used in the production of high- strength and high- performance materials , some of their application include aerospace, development of structural materials, in industries **[41]** and electrical application **[75].**

I.6.2.1. ceramic matrix nanocomposites (CMNCs):

Ceramic nanocomposites are materials composed of ceramic fibers embeded within a ceramic matrix, resulting in fiber- reinforced ceramic materials with enhanced mechanical and structural properties **[77]** where ceramic constitute the major component of their composition **[72]** this type is characterized by a brittle structure and high susceptibility to fracture **[40]** to improve ceramics, making them fracture- resistant and less brittle, reinforcing materials such as fiber, whiskers and platelets can be incorporated to enhance their mechanical performance, or through phase transformation or the use of acrach – bridging mechanism, of this is they of aluminum/ silicon carbide (Al_2O_3/Sic) **[78],** where ceramic matrix nanocomposites based on the aluminum oxide / silicon carbide system exhibit high efficiency and performance, along with a wide range of applications **[7].** Ceramic materials also include carbon, carbon fibers and carbon nanotube with the latter playing a significant role in the advancement of ceramic composites **[72,78]** these materials synthesized using various method and techniques, including sol – gel process are, precipitation, spray pyrolysis polymer

process are , colloidal, template synthesis, conventional powder methode and chemical / physical vapor deposition techniques**[7].**

I.6.2.2. Polymer matrix nanocomposites (pmncs) :

It is a designed material that incorporates nanomaterials uniformly and homogeneously dispersed within a polymeric matrix **[7]** the incorporation of the polymer, including its thermal resistance, biodegradability, mechanical and chemical properties, or it can induce new properties beyond these of polymer, which are acquired form the addition nanomaterials, in all cases, this approach enables the production of high – performance materials with enhanced efficiency while retaining key and new properties pf the matrix **[72,79].** Improvement or the generation of new properties can only be achieved through proper homogenization, ensuring that nanomaterials are uniformly dispersed within the polymer matrix, this uniform distribution is essential for obtaining a polymeric matrix with carbon nanotube, graphene, molybdenum disulfides and tungsten disulfide for reinforcing optimal and effective properties **[80]** it can used polymeric matrix nanocomposites and making it biodegradable **[72]** these materials are characterized by property such as optical activity, conductivity, toughness, mechanical strength, sensing, biological , catalytic activity and thermal stability **[79],** these properties are related to the size, shape, interaction of matrix with nanofiber and type of matrix **[80]** there are various methods for synthesizing polymer matrix nanocomposite, including the sol – gel method. In – situ intercalation polymerization, melt intercalation, direct mixture of polymer and particulates, template synthesis and in- situ polymerization **[41]** these materials offer great potential, making them suitable for a wide range of application such as in electronics, energy storage **[7],** civil in dusty, biomedical and in automotive industry **[81].**

I.7.Polymer – nanoparticles:

I.7.1. Polymer

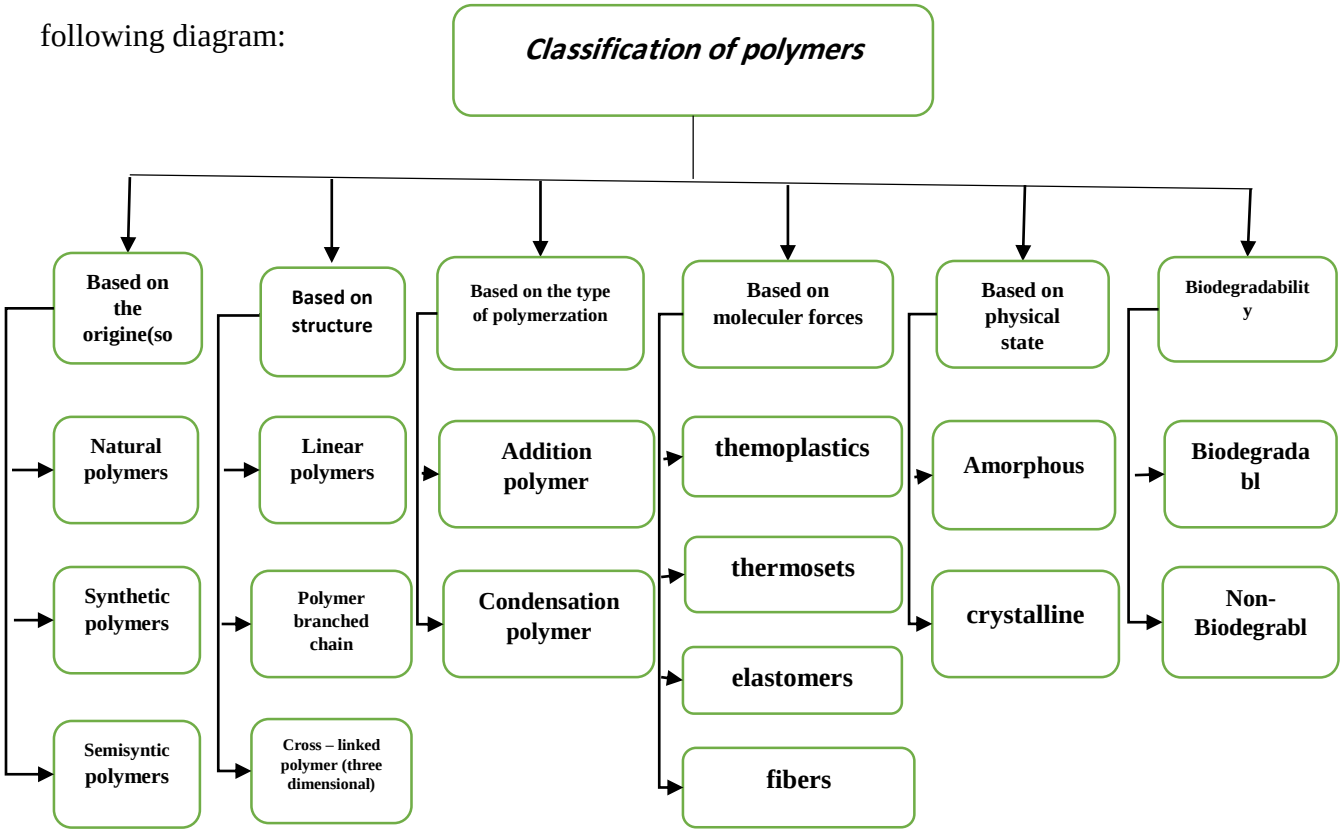
I.7.1.1. Definition :

A polymer is a chemical compound consisting of a macromolecule formed by a large number of small repeating units, giving it a high molecular mass, these small units known as monomer, are bonded to form the polymer structure where each monomer and fictional macromolecule **[82],** therefore, the word “polymer” is a combination of two words, consist of structural components to create a stable poly which means multiple or many and mer means unit or part, the repeating unite or “monomers” linked by covalent bonds **[83].** Polymers are syntheses through a process called polymerization, which is a chemical reaction that leads to the joining of molecules, in this process monemers are selected and linked form the polymer **[82]** a polymer possesses optical properties it is light refraction and

reflection and transmission, electrical properties, mechanical properties **[84],** thermal properties, transport and biological properties. This has given it wide range of applications, including its uses in: clothing, transportation, food packaging, medical care**[85]**

I.7.1.2. Classification of polymer :

Polymer can be classified into various types based on their source, structure, polymerization process, molecualer forces **[82],** physical state and biodegradability. All these type are illustrated in the following diagram:



Schema I.1. polymer types and their classifications

a. Natural polymers :

Natural polymers are compounds that belong to biological systemes **[86]** the source of natural polymers varies allowing them to be classified based on their origine , plant – based polymer where include cellulose, hemicellulose, gluconanman and alginate, also there is animal – based polymers such as gilatine, citoshen, carageenans and dsyllium **[87]** . natural polymers are produced by all living organisns and have no negative impact on the environment **[88]** these polymers are extracte through separation processes, which are often complex and involve multiple steps, it can be categorized into polysaccharides and proteins **[89].**

The variation in natural polymer sources hasgiven it distinct chemical, biological and physical properties. In addition to its biocompatibility and non – toxicity **[86,89].** Due to this properties natural

polymers have large applications, it has been applied in: biomedical field and pharmaceutical it developed and utilized to manufacture patohes for drug delivery and woumd healing and microneedles for drug delivery and applied as additives in food product, energy storage and electronics **[86].**

- **Alginates :**

- **Definition :**

Alginate is a hetrogeneous, linear, anionic ,an hydrophilic polysaccharide found in brown seaweeds and marine algae , it can also be present in certain types of soil bacteria **[87,90].**

The arrangement of monomers within the chain and their molecular weight play a crucial role in determining the physical and chemical properties, of alginate, as well as variations in its structural framework **[90].** Alginate is classified as a carbohydrat drat polymer that serves as a structural component of brown algae cell wall, it consists of sodium, magnesium and potassium salts **[91],** which are formed by converting alginate acid into its salts **[87]** alginate is prepared by extracting broom seaweed after drying and grinding it and using a mineral acid, this step leads to the production of alginic acide in the form of insoluble residues . these residues are then treated with an alkaline solution to convert alginic acide into alginate , which is then precipitated, separated and finally purified **[90].**

- **Structure :**

$\beta-$ D mannwromic acide and $\alpha-$ L $-$guluronic acide linked in $\alpha-$ or $\beta-1,4$ glycosidic bonds as blokes of only $\beta-$ D manwromic acide or $\alpha-L-$guluronic acide in hyompolymer or alternating the two in hetropolymeric boloks **[87].**

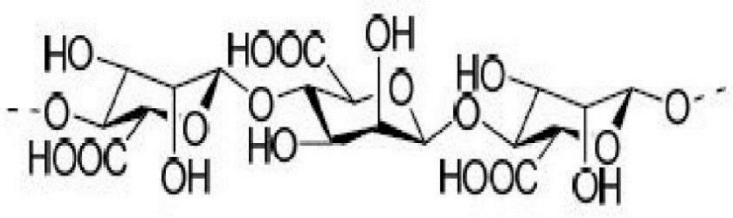


Fig I.10.chemical structure of alginate polymer.

- **Properties :**

- Physical and chemical properties **[90].**

- Alginate have hydrophilicity property.
- Alginate are non – toxic compound.
- Gel – forming ability.
- Solubility, where its solubility depend on its chemical from and PH variation.
- Alginate is a biocompatible compound, as it does not induce a toxic effects.
- That are immunogencity, sterilization an bioadhesion **[91].**

- **Applications:**

- Used as stabilizers in emulsions, suspending agents and tablet disinter grants **[87].**
- Used to controlled drug delivery, wound dressing.
- Cosmetics application.
- Textile industry application.
- Welding rods.
- Food industy application **[91].**
- Biomedical field.

I.7.2. Nanoparticles :

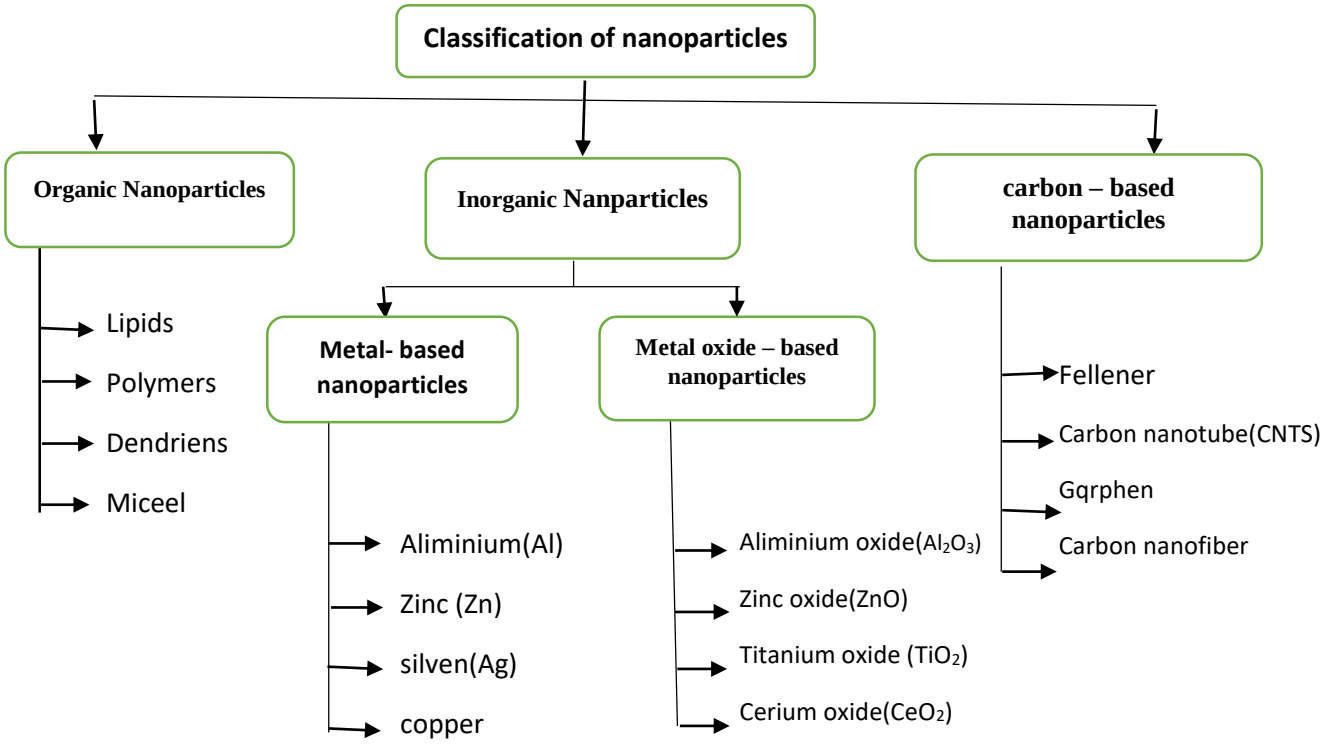
I.7.2.1. Definition:

Nanoparticles are particles composed of materials at nanoscale, ranging between 1 and 100nm they are considered highly precise materials, classifying then as subclasses of colloidal particles **[92]** these materials can naturally occur in phenomena such as volcanoes and wilds fires **[73]** .the shape, size and structure are different in such nanoparticles **[93],** where nanoparticles can be classified into categories based on their size, spherical nanoparticles have all three dimensions in the nanoscale rang, whereas cylindrical tubes take nanoparticles possess two nanoscale dimensions. In contrast, flat or nanoplates have only one nanoscale dimension **[73]** also some nanoparticle can be crystalline or amorphous, this is due to their structure **[93].** The nanoparticle is divided into a surface, a sell materials and a core nanoparticles are generally associated with their fundamental components, which determine their properties **[92]** the components of nanoparticles and their surface area are key factors in determine their properties **[73].**nanoparticle exhibit various characteristics, including: optical, mechanical, hydrophobicity, hydrophobicity, magnetic and electrical properties , reactivity, sensitivity, antibacterial, anti – fungal and toxicity **[93].** Nanoparticles have attracted significant attention, leading to their extensive applications across various fields, medicine and pharmaceutical application where by modifying the surface and size of nanoparticles, they have been utilized for drug delivery purposes enabling controlled drug releases and facilitating drug transport across cellular barriers **[94],** electronics energy, environemental rendiaton **[95].**

I.7.2.2. Classification of nanoparticles:

Nanoparticles are classified according to the compositions into three class: organic, inorganic and carbon – based nanoparticles **[94,95].**

The following shema illustrates the different type of nanoparticles.



Schema I.2. type and classifications of nanoparticles.

I.7.2.3. Nanoparticles with metal oxide based:

Nanoparticles with metal oxide – based composition are particles composed of metals capable of transforming into metal oxide **[94].** These materials, when compared to metal – based nanoparticles, exhibit superior properties, as they are more reactive and possess higher efficiency **[95]** these materials have been designed to modify and enhance nanoparticles composed of metal oxide – specific metals, because in the presence of oxygen, the effectiveness of metal oxides increases compared to the metal **[93].** Some metals have the ability to from group of oxides with different shapes and electronic structure, with grant them semiconducting or insulating properties **[96]** in addition. The structure and composition play role in their water solubility, these particles partially dissolve in water, leading to the formation of new crystalline phases and morphology **[97]** this materials have chemical , electronic, magnetic **[32],** optical transport, mechanical properties **[97].** Nanoparticles with metal oxide – based are have strong applications such as in electronics, energy,

environment, catalysis, biomedical and medicine field **[32]** where have antibacterial properties, this is due to the metal oxides they are composed of, making then more widely used in the medical field, especially in the fabrication of drug delivery **[97].** Nanoparticles oxide metallic include: magnetic and iron oxide (Fe_2O_3)(Fe_3O_4) NPs, silicon dioxide(SiO_2) NPs, zinc oxide(ZnO) NPs, cerium dioxide (CeO_2) NPs, Aluminum oxide (Al_2O_3) NPs and titanium dioxide(TiO_2)NPs **[97].**

- **Zinc oxide nanoparticles (ZnO NPs) :**

Zinc oxide nanoparticles is an inorganic compound that is soluble in water, it exists as a white powder with a crystalline structure, where its crystals are of the wurtizite type **[98,99],** this type has hexagonal structure with two lattice parameters called a and c , the structure consist of two interpenetrating hexagonal sublattices , each containing zinc and oxygen atoms. These two sublattices are displaced relative to each other along the triad C- axis **[100].** Structural variations at the nanoxale of zinc oxide ZnO NPs enable the production of various morphologies, including: nanowires, nanotubes, hollow micro- and nanospheres, nanocolumns, nanosheet, nanobles, nanoflower and nanoords **[28].** Organic compounds or polymers can be used to modify ZnO NPs**[99],** zinc oxide is also considered as semiconductor compound and in addition, possesses an electronic binding energy **[101],** zinc oxide nanoparticles powder is used as an additive in various materials and compounds such as glass, rubber, plastics, ceramics and cement atc. As these addition import new and more effective properties **[99].** ZnO NPs are Charactized by their small size and large surface area **[98].**

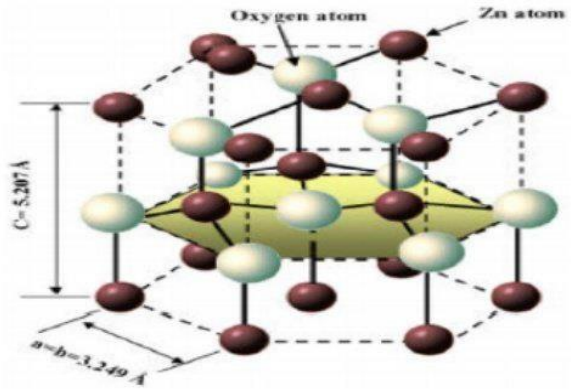


Fig I.11. showen the structure of zinc oxide nanoparticles.

Table I.2. comprehensive overview of zinc oxide.

Properties of ZnO NPs	- Thermal and chemical stability, electrical, optical and mechanical properties **[102].** - Non- toxic materials **[101].** - Have magnetic properties **[28].** - It is antibacterial compounds **[98].** - ZnO NPs are bicompatible, low cost, eco – friendl **[99].**
Methode of syntheses ZnO NPs	- **Physical methodes:** magnetron sputtering, electrodeposition, electron beam evaporation and pulsed laser deposition. - **Chemical methodes:** hydrothermal , solvethermal, chemical bath desposition, precipition, spary pyrolysis and sol – gel. - **Grren methodes:** used plant or microbe medicated **[102].**
Characterization of ZnO NPs	- X-ray diffractometry (XRD), transmission electron microscopy (TEM)m UV6 visible spectroscopy , dynamic light scattering (DLS), scaning electron microscopy, fourmier transform infraref spectroscopy (FTiR), thermogravitic analysis (TGA), X-ray photoelectron spectroscopy (XPS).
Application of ZnO NPs	- Electronics, environmental remediation, optical and electrical devices**[102].** - Used in optolectronics processes. - Solar cells, sensor, photocatalytic, photoluminexense and cosmetic application **[100].** - In pharmaceutical , thus being a non – toxic compound it has been widely usad for drug delivery into body to target the site of infection **[102,101].**

I.7.2.4. Metallic nanoparticles :

Starting from primary mineral materials, pur metallic nanoparticles are produced using the constructive or destructor processes **[94]** metals such as aluminum (al),cobalt(co), copper(cu), iron(fe), silver(ag), zinc(zn), lead(pb), are among the metals used in the production of metallic nanoparticles **[31].** Transition are among the best metals for forming nanoparticles, as they exhibit significant oxidation and reductive activity, this facilitates the formation of metallic nanoparticles **[95],** these nanoparticles exhibit various properties, including their high surface area to volume ration,

pore size, crystalline structure, color **[31].** In addition by high melting points, conductivity, solidity and drigh shine **[101].** Metals also have plasmon resonance, which imports unique optical, electrical and optelectrical properties to metallic nanoparticles **[94],** these nanoparticles exist in spherical and crylindrical fromes, as they are known that are sensitive to environemental factors such as air and heat **[95]** metallic nanoparticles have flexible structure and their behavior and properties depend on their size, these nanoparticles, are present in various application. Due to their nano- toxicity and biocompatibility they have been used in drug, gene delivery, in addition are applied in cosmetics, wound dressings, in biosensing devices **[101],**biomedical application ,catalytic and environmental application.

- **Silver Nanoparticles:**

Table I.3. overview of silver nanoparticles.

Definition and properties of Ag NPs	- Ag NPs are aggregates of silver atoms or ions forming a nanoscale particle with a size ranging between 1 and 100 nm **[103].** - They exhibit distinctive optical, magnetic, electrical **[104],** chemical, physical, thermal and biological **[105].** - Ag NPs have antibacterial activity, where ionic silver is responsible for this activity as it binds to bacterial celles **[94,104].** - Its small size and high surface area provide it with a large surface energy and reactive sites**[106].**
Methodes of synthes Ag NPs	- Chemical method: using chemical reduction. - Physical method: using evaporation and condensation. - Biological method: by green synthesis (plants).
Characterization of Ag NPs	- X-ray diffractiometry (XRD), UV- visible spectroscopy, dynamic light scattering (DLS), Fournier transform infrared spectroscopy (FTIR), X-Ray photoelectron (XPS) scanning and transmission electron microscopy (TEM and SEM)atomic force microscopy (AFM)**[107].**
Application of Ag NPS	- Antibaceterial and anticancer agents, medical device coatings, healthcare, in pharmaceutical industry, drug deliver **[105].** - Anti – inflammatory and anti- fungal activity **[107].** - In fabrication of then - film transitor electrods, optoelectronics, stroge devices **[106].** - In diagnostic and gene therapy and are anti – viral.

I.5.2.3. Green syntheses:

Green synthesis, also known as biological syntheses is an environmentally friendly, safer and biocompatible approaches to producing nanoparticles, this method relies on the use of natural

materials including microorganisms such as bacteria and fungi, or plant – based sources, for the sustainable synthesis of nanoparticles **[108,109]** this methods provides nanoparticles with fewer defects, in addition to their chemically homogeneous composition **[110].** The green method belongs to a bottom -up approach and is based on reduction and oxidation reactions where the substances present in plants or microorganisms are responsible for reducing metals into metallic particles **[109].**as they facilitate reduction or stabilization this makes the method effective, avoiding the use of toxic chemicals end being cost – efficient **[110].** The green syntheses method relies on three main conditions for nanoparticle synthesis : a reducing agent that is environmentally harmless, a solvent and a stabilizing agent that is non – toxic and safe **[108],** this nanoparticles possess antibacterial, anti – fungi, anti – parostic properties **[110]** in addition enhanced biological activity, high stability, sustained drug release and ultrasmall size.

The production of nanoparticles through the green synthesis method using plants involves the utilization of all plant parts, including leaves, stems, seeds, roots and bark, which contain bioactive compounds responsible for the reduction and stabilization processes **[108].** These compounded are plant – derived metabolites, such as trapenoids, sugars, proteins and alkaloids **[49].**

The use of plants in the method is highly efficient, in addition to being a one – step process, the synthesis of nanoparticles is influenced by factors related to the plant source, the compound it contains and concentration of the precursor natural **[109].** In addition, the properties of nanoparticles are determined by the properties an acquired from the plant. Green syntheses are applied in the medicine field to produce drug delivery and in vitro diagnostic application, in treatment of water **[110],** green catalysis, in agriculture and in biodegradable nanomaterials.the mechanism of this method is illustrated in the schema below.

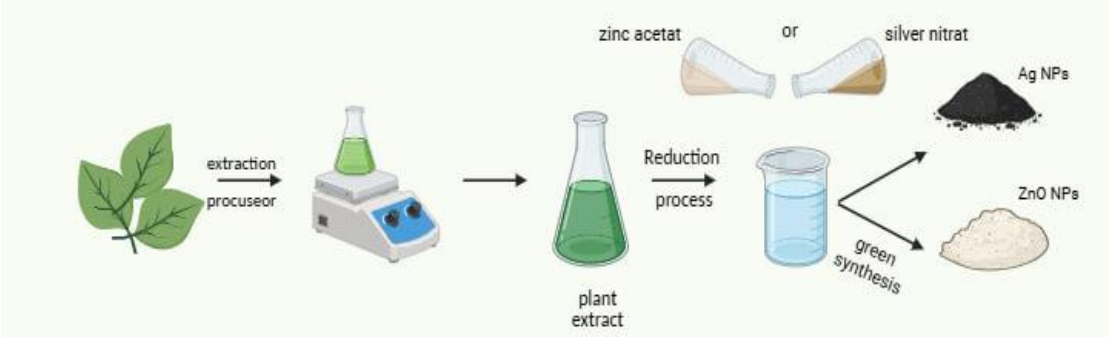


Fig I.12.shema illustrating the mechanism of green synthesis using the plants.

I.7.3. Application of polymeric nanoparticle :

- Environnementale application : water Tratenent application **[111],** biodegradable plastics.

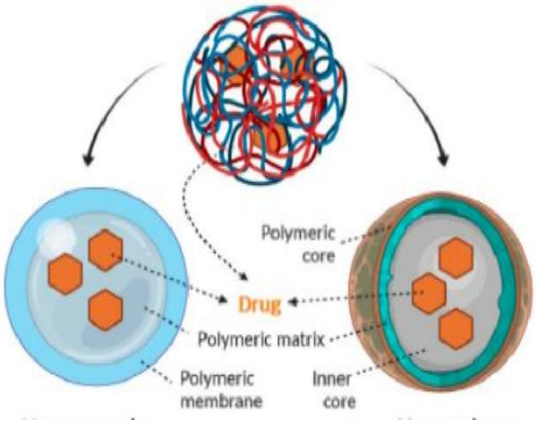
- Agriculture application : nano – fertilisez, nano – fongicides.
- Medical and pharmaceutical application: targeted drug delivery, anticancer therapies, cardiovascular disease, vaccines and gene therapy **[112],** wound healing and tissue engineering.
- Catalysis application **[111].**
- Sensors device **[111].**
- Food packaging and preservation.
- Cosmetics and skincare.

I.7.3.1. Drug delivery:

The conventional drug delivery approach relies on the circulatory system, resulting in only a small fraction of drug reaching the affected area, additionally, this method many cause damage to healthy cells. therefore, a drug delivery system has been developed using nanotechnology, employing nanomaterials capable of drug storage, possessing high solubility and pharmacokinetic properties, in addition to their ability to control drug release to the targeted site, biodegradable polymers, fine nanoparticles, carbon nanotube and other nanomaterials have been used as drug delivery systems, these systems have been used in treatment of diabetes, cancers, tumors and viral infections **[7,113].**

Drug delivery using polymeric nanoparticles is an effective approach, as the drug is transported to the target site either through the swelling of polymeric nanoparticles, followed by drug release, or via an enzymatic reaction that degrades the polymer leading to drug release.

Alternatively, the drug may dissociate from the polymer at the site and be absorbed, this mechanism enables nanotechnology - Based drug delivery to penetrate cells and eliminate then **[114].** Polymeric nanoparticle drug delivery systems are distinguished by their chemical diversity and biocompatibility , these nanoparticles exhibit biodegradability, high therapeutic efficacy, excellent excellent drug – loading capacity and the ability to penetrate biological barriers while maintaining stability within the body .most importantly, they to enable controlled drug release, it also possible to modify and add new functionalities ti these nanoparticles by incorporating additional functional groups **[115,116].**nanoparticles can be nanocapsules and nanospheres **[111]** nanospheres are a polymeric matrix or network that allows the drug to be either encapsulated within or absorbed onto its surface . on the other hand, nanocapsules are surrounded by a polymeric membrane in nanocapsule precisely and consistently controls the release of the drug **[111 , 116].**



Capsule **sphere**

Fig I.13. Two different type of drug delivery made from polymeric nanoparticles.

I.7.4. ZnO NPs – Alginate Beads:

I.7.4.1. Definition:

Zinc oxide nanoparticles – Alginate is the result of combining the alginate polymer with zinc oxide nanoparticles to provide new and effective properties alongside the intrinsic characteristics of both alginate and zinc oxide, with changes in the physical, chemical and biological properties of the resulting material.

It has been found that combing ZnO NPs with alginate leads to the degradation and release of Zn^{2+} ions in the resulting materials, these ions contribute to increased antibacterial activity. additionally, the presence of ZnO with alginate enhances tissue formation and healing, therapy improving the overall mechanical properties of the alginate polymer **[117].** This combination strengthens electrostatic interaction and hydrogen bonds between zinc oxide nanoparticles and the polysaccharide present in alginate, increases the antibacterial properties with the stabilization of zinc oxide nanoparticles **[118].** This technique has been used in various applications, such as polymeric and nanotechnology – based systemes, which aim to drug formulation and delivery, in addition to controlling drug release, the interaction between ZnO NPs and alginate may lead to the formation of a cohesive polymeric network enabling a gradual drug release (enhancing the anti – cancer repose).

it has also been used in environmental application, where developed into devices for water treatment **[118].** The following schema further illustrates the formation and release of the beads.

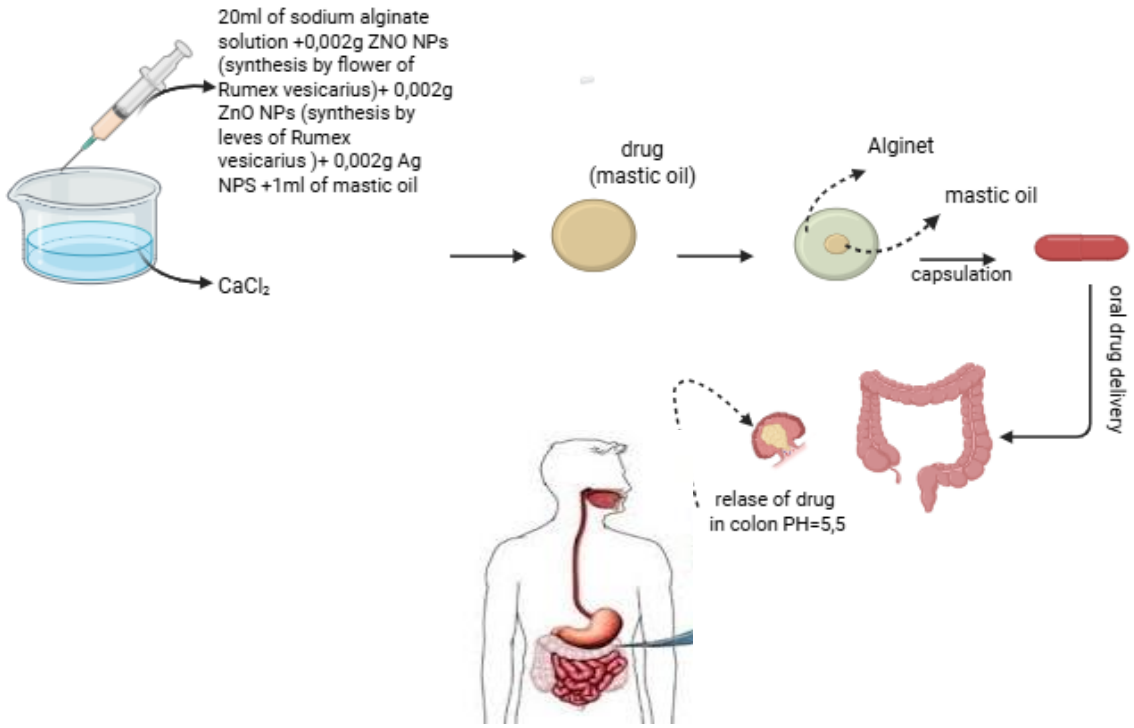


Fig I.14. illustrative diagram of the formation of the drug carrier and its oral administration pathway to colon for targeted drug release

I.7.4.2.Mechanism of drug release:

Drug release, i.e, the release of the active substance, occurs through three different mechanisems or systems **[119,120]** :

a. **Extended release:** this system enables the prolonged release of the drug, as it is designed to extend the duration of active substance delivery within the body. The total dose is retained by embedding it in a material that is insoluble in bodily fluids, allowing the active ingredient to be released slowly oven time **[119]** among the materials used in this system is polymer matrix, through which drug release accurse either by diffusion alone or by swelling followed by diffusion **[120]** the extended – release system is designed to prolong the therapeutic effect by continuously releasing the drug oven an extended period **[121].** The use of this system helps avoid drug Sid effects by maintaining an effective drug concentration for a longer duration and preventing its fluctuation in the body **[122].**

b. **Controlled release:** it is an advanced system in which the drug is released at a specific rate with precise control and at defined intervals in addition to controlling the site of active substance release within the body. This system is administered orally and is suitable for repeated dosing **[123].** In this system, a constant drug level is maintained either on the blood or in the target cells, which is attributed to its programmed release **[121]** it is also classified into several categories, such as to enhance drug efficacy, reduce side effects,and relulate adregulat patient compliance with medication **[124].**

c. **Immediate release:** this system is characterized by the rapid and direct release of the active substance immediately after administration, and in a simple manner **[125]** in this system the release rate cannot be controlled and it can be dissolved prior to administration in water or certain solvents **[126].** Alternatively, rapid disintegration of the tablet are capsules may accrue within the stomach or biological finds. These mechanisms are summarized in the following curve.

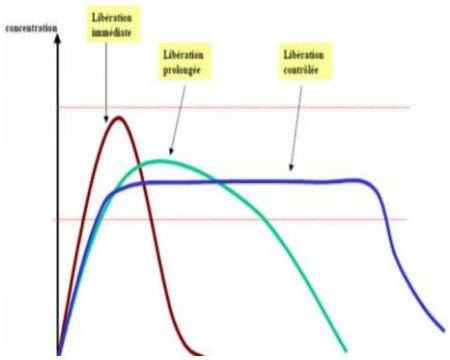


Fig I.15. classification curve of drug release patterns : controlled, immediate and extended [120] .

Chapter II

Experimental Section

II.1.**Introduction:**

In the field of striving to develop effective nanotherapeutic systems based on natural foundations derived from medical plants, this experimental work involved the preparation of pharmaceutical formulations and therapeutic dressings based on nanoparticles synthesized from plants with medicinal properties.

The experimental work involved of zinc oxide nanoparticles (ZnO NPs) and silver nanoparticles (Ag NPs) using the green method, with *Rumex vesicarius* plant used as reducing and stabilizing agent this was done with the aim of using them as nanopharmaceutical compound in the form of drug delivery particles, encapsulated with mastic oil, directed towards cancer treatment based on their anticancer properties.

Nanotherapeutic dressings intended for burn treatment and wound healing were also prepared these dressings were based on zing oxide nanoparticles and silver nanoparticles, synthesized using the *haloxylon Spp* plant due to its actives compounds the help accelerate wound healing and reduce inflammation.

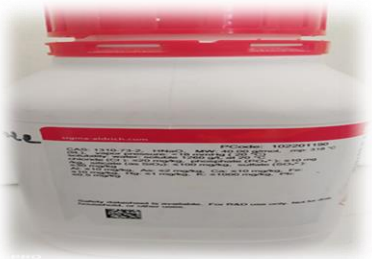
Sodium alginate polymer was used as a matrix for the fabrication of both the drug delivery particles and the therapeutic dressings.

- ***Objective:***

- The formulation of an anticancer drug delivery using *Rumex vesicarius* and mastic oil.
- The development of nanotherapeutic dressings aimed at treating burns and promoting wound healing, using the *haloxylon* Spp and *mastic* oil.

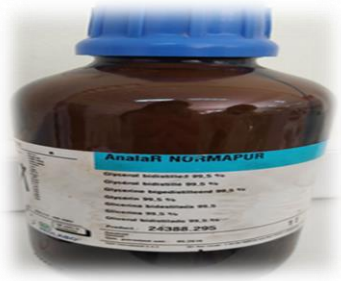
II.2. Chemical and equipment used :

II.2.1. Chemicals: **Tabel II.1.** comperehensive overview of the materials used in the study.

Name	Formula	Molar mass	Picture
sodium hydroxide	**NaOH**	**40 g/mol**	

Zinc acetete dihydrat	**$C_4H_6O_4Zn,(2H_2O)$**	**219.50 g/mol**	
Calcium chloride dihydrate	**$CaCl_2,2H_2O$**	**110.98 g/mol**	
Silven nitrate	**$AgNO_3$**	**169.873g/mol**	
DPPH	**$C_{18}H_{12}N_5O_6$**	**394.317 g/mol**	
Ascorbic acide	**$C_6H_8O_6$**	**176.124g/mol**	

Vitamin B12	**$C_{63}H_{88}CoN_{14}O_{14}P$**	**1355.38g/mol**	
Eetanol	**C_2H_6O**	**46.068g/mol**	
Aceton	**C_3H_6O**	**58.07g/mol**	
Deionied water	**H_2O**	**18.02g/mol**	
Sodium alginate	**$NaC_6H_7O_6$**	**198.1g/mol**	

Glycerol	**$C_3H_8O_3$**	**92.09g/mol**	
Chloroform	**$CHCl_3$**	**119.387g/mol**	

II.2.2. Equipment:

Analytical Balance

Magnetic stirrer

Centrifuge

oven

shaker

microscopie

Fig II.1. Tools and equipment used in the practical part of the study.

II.3. Plant:

- ***Rumex vesicarius :***

Rumex vesicarius is a wild leafy plant belonging to the oleander family, traditionally used in various cultures for medicinal purposes **[127].** This plant contains a variety of bioactive chemical compounds, including anthraquinones, flavonoids, tannins, saponins and alkaloids, known for their important biological properties, such as antioxidants, antiproliferative, and antimicrobial properties **[128].**

Recent studies have shown that plants belonging to the Rumex genus exhibit broad biological activity, including antitumor properties, with proven efficacy against various types of cancer cells, including gastric and colon cancer, melanomas, and other cancer cells. Furthermore, its therapeutic role has been noted in treating gastrointestinal disorders such as vomiting, diarrhea, and gastritis, as well as combating pathogenic bacteria such as Escherichia coli.

Based on this information, this study aimed to evaluate the antimicrobial activity of aqueous extracts from the leaves and flowers of Rumex by analyzing their bioactive effects on selected bacterial strains **[129].**

- ***Haloxylon SPP:***

Haloxylon plant is a wild plant belonging to the Chenopodiaceous family **[130],** and is known in traditional herbal medicine for its antimicrobial and anti-inflammatory properties. This plant is widely used to treat various medical conditions, with traditional studies showing its effectiveness in treating wounds, burns, and purulent ulcers **[131].**

Although the bioactive compounds of this plant have not been fully studied, a variety of active compounds have been identified, including alkaloids, bideranonates, titanates, saponins, and glycosides. These compounds contribute to the therapeutic properties of the plant and show promising potential in medical applications such as infection control and inflammation reduction **[132].**

- ***Mastic Oil* :**

Mastic oil is extracted from the Pistacia lentiscus plant, which belongs to the Anacardiaceae family. This essential oil is rich in several bioactive compounds, notably α-pinene, β-pinene, limonene, and various terpenes. Its volatile fraction also contains important constituents such as β-caryophyllene and germacrene, which are responsible for many of its biological properties**[133].**

Studies have demonstrated that mastic oil possesses strong antioxidant activity, primarily due to its high content of terpenoid compounds. Additionally, it exhibits antibacterial properties by inhibiting the growth of various bacterial strains. The oil also shows anti-inflammatory effects and notable

anticancer potential, as several findings suggest its ability to induce apoptosis in cancer cells and inhibit their proliferation **[134,135].** These combined properties highlight the significance of mastic oil as a promising natural source for pharmaceutical and alternative medicine applications**[135].**

- **Table of biocompound in mastic oil:** the compositional content of mastic oil is presented in the following table, **table II.2.** biocompound present in mastic oil **[133].**

compound	relative area(%)	structure formula	MW
α-pinene	67.71	$C_{10}H_{16}$	136.24
Camphene	0.70	$C_{10}H_{16}$	136.24
Verbenene	0.07	$C_{10}H_{14}$	134.22
β-pinene	3.05	$C_{10}H_{16}$	136.24
Myrcene	18.81	$C_{10}H_{16}$	136.24
Limonene	0.89	$C_{10}H_{16}$	136.24
Linalol	0.73	$C_{10}H_{18}O$	154.25
α-campholenic	0.26	$C_{10}H_{16}O$	152.23
Pinocarveol	0.32	$C_{10}H_{16}O$	152.23
trans-verbenol	0.07	$C_{10}H_{16}O$	152.23
cis-verbenol	0.69	$C_{10}H_{16}O$	152.23
Verbenone	0.32	$C_{10}H_{14}O$	150.22
Caryophyllene	0.50	$C_{15}H_{24}$	204.36

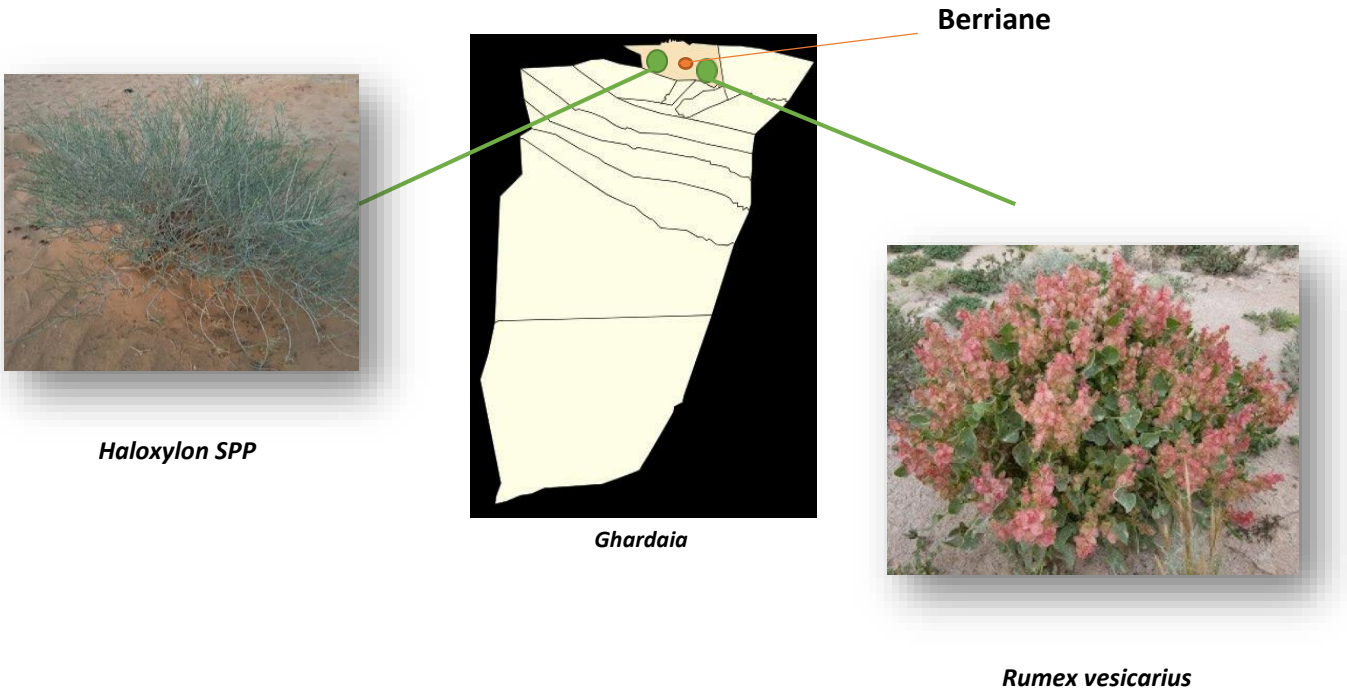


Fig II.2. geographical locations of the used plant sources.

II.4. Experimental proportion protocols:

II.4.1. Preparation of the chemical solution used:

Table II.3.preparation details of solution used in the experiments.

Solution Nome	Concentration (mol/l)	Weighed mass(g)	Preparation volume(ml)	Preparation solvent
Sodium hydroxide (NaOH)	2	8	100	Deionized water
Zinc acetate $Zn(C_2H_3O_2)$	0,1	2,195	100	Deionized water
Calcium chloride($CaCl_2$)	0,5	27,745	500	Deionized water
Silven nitrate solution($AgNO_3$)	10^{-3}	0,017	100	Deionized water
DPPH	$6,07*10^{-4}$	0,024	100	Ethanol
Ascorbic acide	0,005	0,05	50	Deionized water
Vitamine B12	$1,5*10^{-4}$	0,02	100	Deionized water

Observation : after preparing the solution of ascorbic acid and DPPH, they should be stored in a dark environment, wich can be achieved by wrapping them in alumimium fiol to block light.

Fig II.3. visual documentation of the prepared solutions.

II.5. Preparation of plant extracts:

We Washing and drying The plants with water and them placed in an oven to dry completely at a tenperature not exceeding 50℃ then Grinding , after that we prepared the Extracts of plants . for synthesis ZnO NPs, 10 g of plants are placed in 100 ml of deionized water under continuous stirring using a magnetic stirrer for a duration of 15 min at a temperature not exceeding 60℃. But for the Extract of synthesis Ag NPs , where we weigh 2,5 g and placed in 50 ml of deionized water under continuous stirring for duration of 15 min at a temperature [40 - 50]℃. After 15 min , it is left to cool, then filtered to separate the plant from the extract, using filter paper the extraction step are illustrated in the following schema

- **Stages of extracting *rumex vesicarius* :**

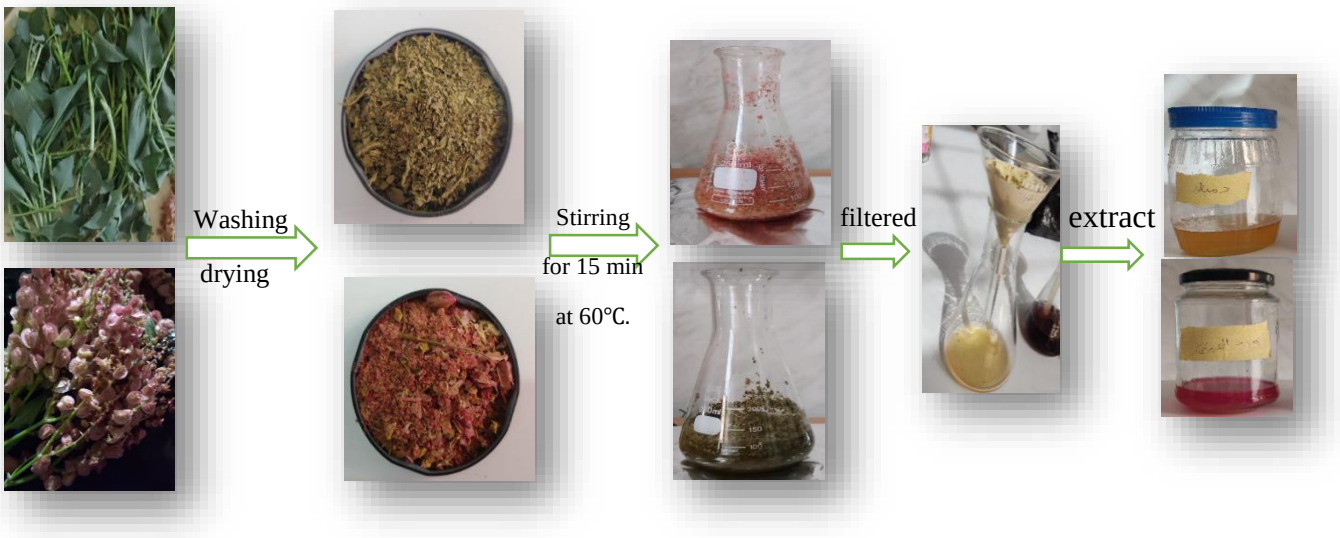


Fig II.4. sequential of the extraction process of *rumex vesicarius*.

- **Stages of extracting *Haloxylon* plant extract:**

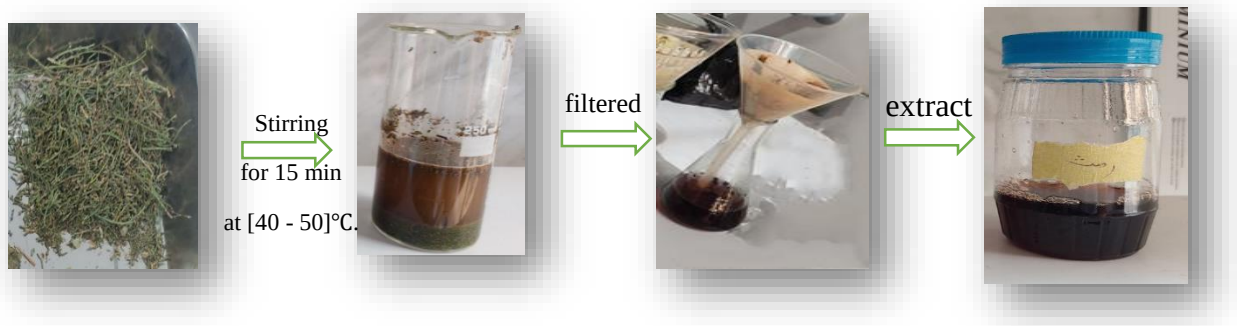


fig II.5. practical workflow for haloxylon SPP plant.

II.6. Synthesis of oxide nanoparticles (ZnO NPs) by green method :

- **by *Rumex vesicarius*:** 80 ml of zinc acetate solution is placed , then 20 ml of *R,vesicarius* extract (flower and leaf extracte separatoly and in the some manner) is gradually added under continuous stirring using a magnetic stirrer for 15 min at temperature not exceeding 40 °C.

Fig II.6. illustration of zinc oxide formation by *R. vesicarius*

- **by *Haloxylon* SPP:**

  80 ml of zinc acetate solution is pleased , then weed gradually 20 ml of *haloxylon* SPP and less then under continuous stirring for 15 min at temperature not exceeding 40 °C .

Fig II.7. illustration of zinc oxide formation by *haloxylon*

PH adjustment: the nanoparticles are formed in a basic medium at a PH of 10. to adjust this value, after 15 min of stirring , drops of sodium hydroxide (NaOH) are added until the PH reaches 10 . (this step is applied in both *haloxylon* SPP and *Rumex vicarious*) where the amount of NaOH added depends on the type of plant used, we using to measure PH value paper of PH. After adjusting the PH value, the mixture is left under continuous string at the same temperature for one hour 1h.

Fig II.8. PH adjustment in a medium allowing for the formation of ZnO NPs.

- **collection of ZnO nanoparticles:**

- After on hour, the mixture is allowed to cool , then transferred into tubes and immediately placed in a centrifuge for 10min at a [4000 - 6000] rpm, in order to separate the zinc oxide nanoparticles from the liquid phase.
- The zinc oxide nanoparticles are washed to ensure their purity. First, deionized water is added to tube containing the ZnO NPs, then the mixture is thoroughly stirred and centrifuged for 10 min. th supernatant is discarded and the process is repeated twic using ethanol . in the final step, distilled water is added again and the same procedure is followed, until pure ZnO NPS are obtained.

- **Drying ZnO NPs:**

- The obtained ZnO NPs are transferred to glass diches and plased in an oven at a temperature of [650 - 700]℃ for on hour. after this step, the zinc oxide nanoparticles are obtaind in the form of a white powder.

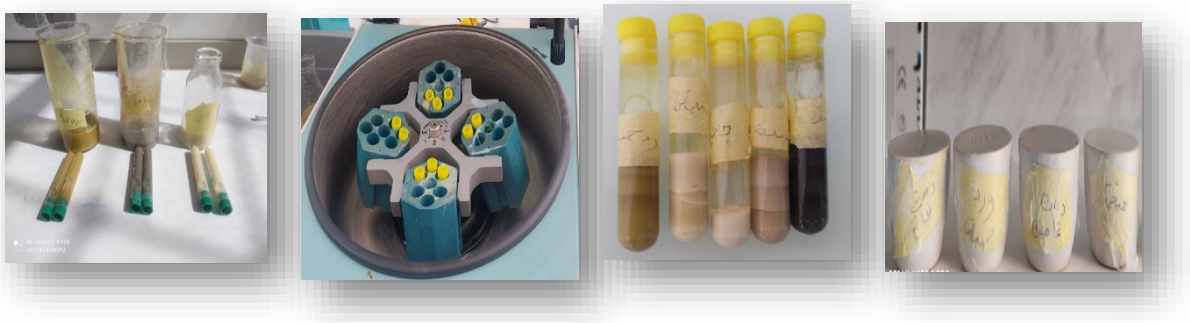


Fig II.9. mechanism of collection, purification and drying of ZnO NPs.

II.7. Synthesis of before proceeding with the green synthesis of silver nanoparticles, a peril silver nanoparticle (Ag NP) by green methode:

II.7.1. verification of the synthesis of silver nanoparticles ysing the employed extracts:

Before proceeding with the green synthesis of silver nanoparticles a preliminary test is conducted to determine which of the used plants are capable of producing silver nanoparticles, the procedure consistes of the following step:

- Preparation of samples with different concentrations:

N tube	**1**	**2**	**3**	**4**	**5**
Volum of extracte ml	1	2	3	4	5
Volume of AgNO3 ml	9	8	7	6	5

- Heating the samples by placing them in a beaker containing then in a beacker contining water for 15 min.
- Selection of the extract based on visual observation and absorbance measurement using a spectraphotometer UV – visible .

- **By flower of *R.vesicarius*:**

90 ml of silver nitrate $AgNO_3$solution is placed in a beaker, which is immersed in a water bath at a temperature not exceeding 40℃ . then, 10 ml of *Rumex vescarius* flower extract is gradually added under continuous stirring for one hour.

Fig II .10. formation of silver NPs by *R. vesicarius*

- **Observation:**

Silver nanoparticles were synthesized using sorrel flower extract, as the leaf extract did not result in nanoparticles formation. This conclusion was reached after conducting a comparative teste.

- **By *Haloxylon* SPP :**

90ml of silver nitrate AgNO3 solution is placed in a beaker , which is immersed in a water bath at a temperature 40℃ .then 10 ml of *haloxylon* extract is gradually added under continuous stirring for 1h.

Fig II .11. formation of silver NPs by *haloxylon*.

- **Collection of Ag NPs:**

- we transferred the mixture after cooling into tube and immediately placed in a centrifuge for 10 min at a [4000 - 6000] rpm.
- The silver nanoparticles are washed to ensure their purity. First deionized water is added to tube containing Ag NPs , then the mixture is thoroughly stireed and centrifuged for 10 min . the supermatant is dixarded and the process is repeated twic using ethanol and the some stepe by deionized water.

- **Drying Ag NPs:**

The obtained silver nanoparticles are placed in a glass disk and then dried in an oven at 600 ℃ for a period ranging for 3 to 4 hours. after this step, the silver nanoparticles are obtained in the form of a dark brown powder.

II.8. preparation of alginate solution:

2g of sodium alginate is weighed and gradually added to 100ml of deinzed water to avoid the formation of lumps and to ensure complete homogenization. The solution is stirred continuously for tow hours, then left to rest for at least 30 mintes before use.

Fig II.12. collection and drying of Ag NPs in their final form.

II.9. Preparation of drug delivery and Mastic Oil beads based on *R.vesicaruis*:

Nanocarrier drug spheres were prepared based on alginate polymer, silver nanoparticles and zinc oxide nanoparticles. Five categories of microspheres were developed , differing either in their composition or in the encapsulated material each of these mixtures is placed in a syring , then fine droplets are carefully released into a calcium chloride solution , which is used to form the drug microspheres by creating cross – links with the alginate polymer, genthe cirocular stirring is maintained during the dropwise addition to facilited the formation of uniform spheres.

❖ **Formulation of the categories:**

1- Alginate spheres:

These spheres are prepared using only sodium alginate solution by directly loading the solution into a syring and forming the spheres.

2- Alginate spheres with nanoparticles:

Within 20 ml of alginate solution, 0,002 g of zinc oxide nanoparticles synthesized from *R.vericarius* flowers and 0,02 g synthesized from leaves are added, followed by the addition of 0,002 g of silver nanoparticles. It is essential to ensure the thorough homogenization of the nanoparticles within the alginate solution.

- This mixture serves as the base and using the same components and proportions, the following microspheres are formelated:

a) Alginate spheres containing only nanoparticles:

They are composed of the base mixture, which includes sodium alginate, silver nanoparticles and zinc oxide nanoparticles .

b) Spheres loaded with Mastic Oil :

1 ml of Mastic Oil is added to the base mixture and mixed thoroughly until a homogenous blend is obtained. The resulting mixture is then used to from the spheres.

c) Spheres loaded with vitamin B12:

0,002 g of vitamin B12 is added to base mixture and thoroughly mixed to ensure homogeneity. The resulting mixture is then used to form he spheres containing vitamin B12.

d) Spheres loaded with ascorbic acide :

0,002 g of ascorbic acid is added to the base mixture and mixed thoroughly to ensure uniform dispersion and homogeneity. The resulting mixture is then used to form spheres encapsulating ascorbic acid

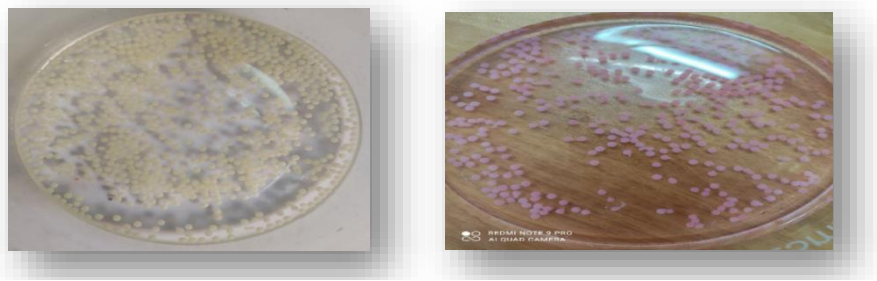


Fig II.13. bead formation via cross – linking reactions in $CaCl_2$

- **Stirring of spheres using lab shaker:**

The formed spheres are gently stirred using lab shaker to fully from and establish stable cross – linking bonds to ensure uniformity and prevent aggregation, as well as to prevent their disintegration.

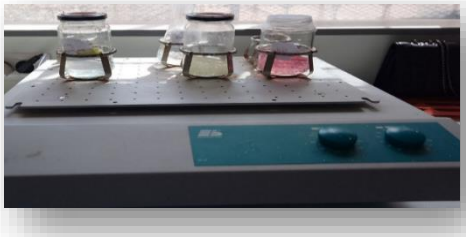


Fig II.14. enhancement of cross – linking using orbital shakier

- **Filtration of the drug – loaded spheres:**

The spheres are filtred to remove the calcium chloride solution using filter paper. The form after filtration is shown in following the images.

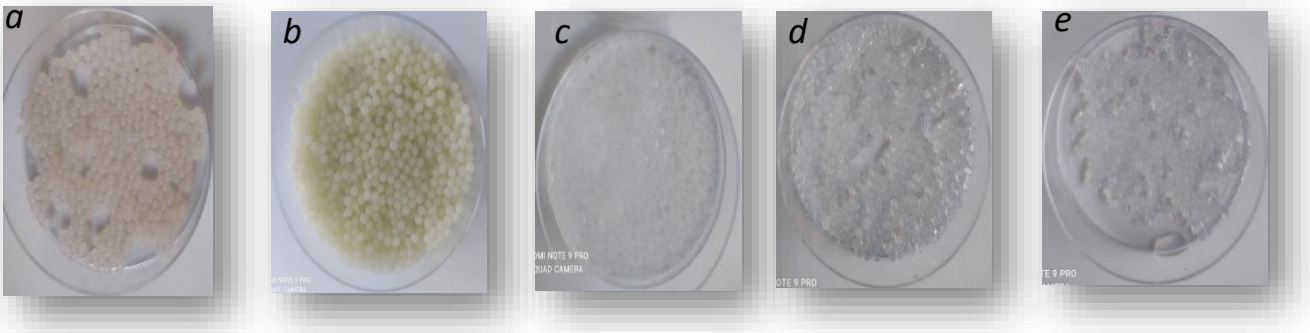


Fig II.15. filtration of drug – loded beads from $CaCl_2$: : (a)V B12, (b) mastic oil,(c) ascorbic acide, (d)spher of alginate with ZnO / Ag NPs.

- **Drug of the spheres:**

After filtration , the spheres are transferred into petri diskes and placed in an oven at 35℃ for on hour until completely dried.

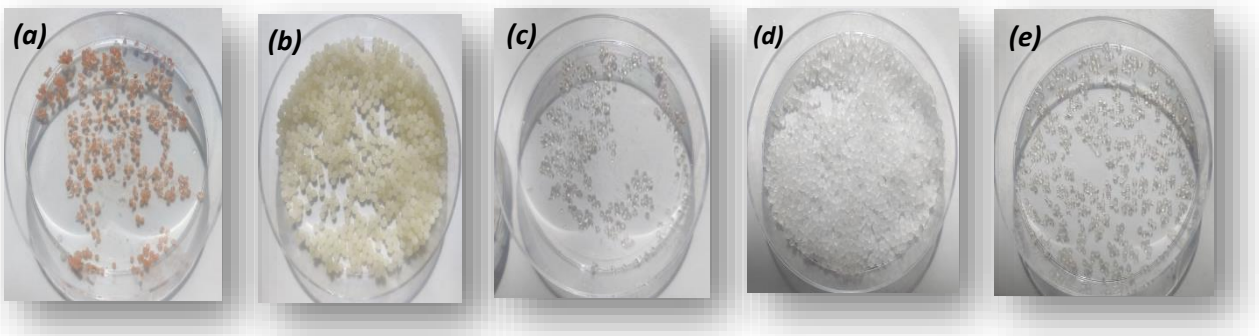


Fig II.16. Finel from of the loaded beads after drying. Spher leoded : (a)V B12, (b) mastic oil,(c) ascorbic acide, (d)spher of alginate with ZnO / Ag NPs.

- **Filling pills into polymer carrier capsules :**

Fig II.17. loaded drug carriers en capsulated in capsules.

II.10. Prparation of therapeatic dressing for burn and wuond healing by *Haloxylon* and mastic oil:

The dressing are prepared using alginate polymer, silver nanoparticles and zinc oxide nanoparticles synthesized from *haloxylon* . based on thes components , different categories of dressings are formulated. Amony these categories, one involves adding mastic oil to the dressing with nanoparticles and alginate, wihile on other involves incorporating *haloxylon* powder with alginate and nanoparticles. The mastic oil is effective in treating,burnsm wihil the *haloxylon* drissing has benefits in wound healing inflammation reduction and treatement of burn scars.

- **The dressings compositino:**

1- Alginate dressing:

The alginate dressing is prepared using alginate polymer as the primary matrix, the alginate solution is directly poured into the mold.

2- Alginate dressing with nanoparticles:

The dressing is prepared by adding 0,002g of silver nanoparticles and 0,002 g of zinc oxide nanoparticles into 20 ml of alginate soloution . followed by thorough mixing to ensure homogeneity if the mixture and poured into mold.

3- Alginate dressing with nanoparticles and containing m.oil:

The dressing is prepared by incorporating 0,002g of Ag NPs and 0,002 g of ZnO NPs into 20 ml of alginate solution, followed by the addition of 1 ml of mastic oil. The mixture is then thoroughly mixed to ensure uniform distribution of the nanoparticles and oil.

4- Alginate dressing with nanoparticles and containg *Haloxylon* SPP powder:

We add 1 g of *haloxylon* SPP powder to the mixture of alginate and nanoparticles and mix thoroughly to ensure complete homogenization of the mixture. The formed mixture is shown in the following images.

Fig II.18. Pre – formalation stage of the wound dressing components.

- **Crosslinking and formation of the dressing:**

After pouring the different mixture into molds, they are immediately placed in the refrigeration and left to cool and solidify completely. Then, they are taken out and left to room temperaturs to melt and return to their initial state. Afterward, they are placed back into the refrigeration. This cycle is repeated three times in order to form strong and cohesive bonds, thus preventing disintegration.

- **Crosslinking with chloride calcium $CaCl_2$:**

They are extracted from the mold and placed in a calcium chloride solution to allow the alginate–based dressing to fully from and establish stable cross – linking bonds .

- **Drying of the dressings:**

After the cross – linking process , the dressings are left in a room until they are completely dried.

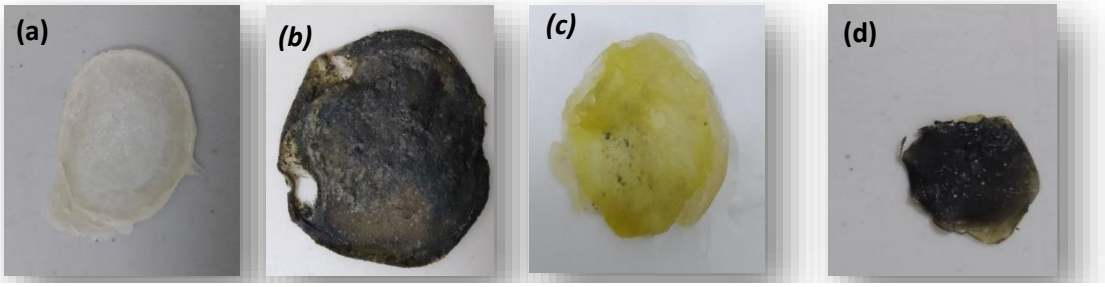


Fig II.19. the dressing in its final dried form (a-d) - alginat dressing, (b)- alginate dressing with NPs and haloxylon powder, (c)- alginate dressing with NPs and mastic oil.

II.11.Characterization :

II.11.1.Characterization of zinc oxide and silver nanoparticles, beads :

II.11.1.1. Spectroscopy UV – Visible:

Ultraviolet-Visible (UV-Vis) Spectroscopy is an analytical technique used to measure the absorption of ultraviolet and visible light by a substance. It is widely used to study the optical and electronic properties of materials, especially nanoparticles **[136].**

Principle :

- Based on the absorption of UV and visible light by a substance.
- The light has enough energy to excite electrons from lower to higher energy levels.
- Each material absorbs specific wavelengths depending on its electronic structure.
- Nanoparticles show a distinct absorption peak due to Surface Plasmon Resonance (SPR).
- The position and intensity of the peak provide information about the nanoparticle's size, shape, and composition.
- The technique helps determine electronic transitions and optical band gaps **[136,137].**

Fig II. 20. UviLine UV-Vis model 9400C

II.11.1.2. X-ray Diffraction (XRD) :

X-ray Diffraction (XRD) is a powerful analytical technique used to study the crystal structure and properties of nanoparticles. It helps determine parameters such as crystallinity, particle size, and lattice strain at the nanoscale by analyzing the diffraction pattern formed when X-rays interact with a crystalline material **[138].**

A Malvern Panalytical XRD instrument was used to study the crystal structure of Ag NPs and ZnO NPs. The instrument was equipped with the LYNXEYE scintillation detector and Cu Kα radiation (λ = 1.54184 Å) at a voltage of 30 KV and a current of 10 mA. The samples were placed in a sample

holder and scanned over a range of 25 – 40° with a step size of 0.0202° at 1 s per step (1733 steps in total) and rotated at 15 rpm to obtain an average diffractogram of the samples.

Principle :

- Uses monochromatic X-rays with short wavelengths (0.01–10 Å).
- When directed at a crystalline sample, X-rays interact with atomic planes in the crystal.
- The interaction causes scattering of X-rays in various directions.
- These scattered rays produce a diffraction pattern based on the atomic arrangement.
- Angles and intensities of diffraction peaks reveal:

Crystal structure

Atomic spacing (distance between planes)

Crystallite size and strain

- The diffraction follows Bragg's Law, which relates the angle of incidence to the spacing between atomic layers.
- XRD is non-destructive, precise, and widely used in nanoparticle characterization **[149].**

Fig II.21. Malvern Panalytical model diffractometer.

II.11.1.3. scanning electron microscopy:

Scanning Electron Microscopy (SEM) combined is a dual technique used for high-resolution imaging and elemental analysis of nanoparticles. SEM provides detailed surface morphology, while EDX identifies the elemental composition of specific regions or points on the sample**[140].**

Principle:

Scanning Electron Microscopy (SEM):

- A focused electron beam scans the surface of the nanoparticle sample.
- The interaction of the beam with the sample produces:

Secondary electrons (used for imaging).

Backscattered electrons (for contrast and composition).

These signals create high-resolution images showing:

Surface morphology

Shape and size

Distribution of nanoparticles

Energy-Dispersive X-ray Spectroscopy (EDS):

The electron beam ejects inner-shell electrons from atoms in the sample.

- Characteristic X-rays are emitted as outer electrons fill the vacancies.
- These X-rays are element-specific, allowing:

Elemental identification

Quantitative analysis

- EDS detects and analyzes these X-rays to determine the elemental composition of nanoparticles **[141].**

II.11.2. Application teste :

II.11.2.1. Antioxidant activity teste:

This test is used to evaluate a substance or compound for its ability to resist oxidation or combat free radicals, which can cause damage to cells and tissues. In our work, this test was employed to assess the antioxidant capacity of the synthesized nanotherapeutic compounds designed to protect cells from oxidative stress, with the aim of combating cancer and promoting skin healing.

The DPPH method was selected for the antioxidant activity test this method is based on the ability of antioxidants to reduce the DPPH free radical, wich is a stable radical with a purple color, upon reduction, it becomes either colorless or play yellow, leading to a decrease in absorbance measured at a wavelength of 517 nm, following the protocol , 24mg of 2,2 – diphenyl -&- picrylhydrozl (DPPH) were weighed and dissolved in 100 ml of ethanol with then prepared for subsequent comparison by mixing 1 ml of the dpph solution with 1ml of ethanol. As previously noted to dpph solution is charactezed by its purple color, this color disappears when an antioxidant agent is present in the reaction medium.

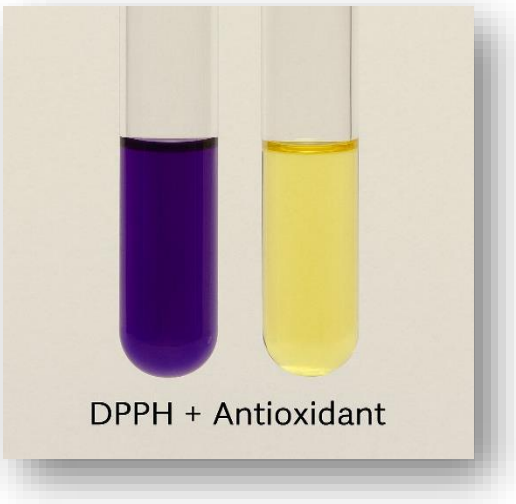


Fig II.22. Color change of DPPH as an indicator of antioxidant activity.

The samples to be tested for antioxidant activit are firset prepared then , 1ml form each sample is mixed with 1ml of DPPH solution and incubated in the dark for one hour, after incubation, the absorbance of both the sample and control solution is measured at 517 nm.

The antioxidant activity is expressed as a percentage of DPPH radical inhibition according to following equation **[143]**.

$$(\%\ of\ inhibition = ((A_0 - A_{teste}) / A_0 \times 100) \ldots\ldots\ldots\ldots (1)$$

Indice : $A_0 - A_{teste}$

Ou:

A_0: Absorbance of the control solution.

A_{test}: Absorbance of solution teste.

- We divided our work in measuring antioxidant activity into absorbance measurement of the following materials.

a. Ascorbic acid + DPPH essay:

It was used as reference antioxidant compound to compare the effectiveness of the tested materials and the drug – loaded beads. This provides a baseline for comparison.

b. Measurement of the extracte:

To evaluated their effectiveness as natural antioxidant and to determine whether they possess antioxidant activity.

c. Measurement of mastic oil:

In order to test the antioxidant capacity of mastic oil , the evaluation was carried out based on its richness in phenolic compounds and antioxidant agents. This allous for assessing its role in protecting cells and contributing to oxidative stability.

d. Evaluation of the antioxidant activity of nano drug- loaded beads:

Evalution of the ability of nanostructured formulations to gradually release active compounds over time without losing their antioxidant properties in a physiologically simulated environment using a buffer solution at PH = 5.

e. Evaluation of the antioxidant activity of the nanoparticles:

It allows determining their biological activity as antioxidants additionally, it aims to verify whether these particles, prepared using green methods with plant extracts, retain active compounds on their surface and to assess their potential use in therapeutic applications related to oxidative stress.

II.11.2. Method of preparation for antioxidant test:

- **Preparation sample of ascorbic acide, extracts and mastic oil:**

In these measurments, we relied on preparing solution with different concentrations of the samples and varying volumes for each solution? After preparing the sample (extractes, mastic oil and ascorbic acide), 1ml of each sample is taken after the dilution and placed in a test tube with 1 ml of DPPH solution. The samples are then kept in a dark environement for one hour.

the control solution is considred a reference in calculating the antioxidant activity. It is prepared by mixing 1 ml of DPPH solusion with 1 ml of ethanol to measure the absorbance and determine the percentage of inhibition. The absorbance of the control solution is denoted as A_0.

Fig II.23. Control Sample Tube of the antioxidant activity

- **Preparation of nanoparticles sample:**

We take 0,002 g of each previously synthesized nanomaterial (silver nanoparticles and zinc oxide nanoparticles) derived from rumex vesicarius and haloxylon SPP separately in test tube. Then, 1 ml of ethanol is added to each tube and mixed thoroughly to dissolve the nanoparticle. After that, 1 ml of DPPH solution is added and the mixtures are kept in the dark for one hour.

- **Absorbance measurement :**

- We use a UV – visible spectrophotometer to measure the absorbance, after determining the absorbance, the inhibition percentage is calculated and used as a basis for evaluation where: Table II.6. Classification of Antioxidant Activity Based on Inhibition Percentages **[144]**

% inhibition	Above 70%	[40,70] %	Less than 40%
value analysis	Strong antioxydant activity	Moderate antioxydant activity	Weak antioxidant activity

We also rely on the value of IC50, where the lower the IC50 value, the stronger the antioxidant activity.

II.11.4. Release test:

a. **Preparation of sample for the evaluation of nanocarrier drug spheres :** We prepare a saline solution by adding a small amount of buffer powder PH = 5 – 7,5 (simulate the PH of the colon) to 30 ml of deionized water. The solution is then divided into three beakers, with each type of green – synthesized drug – loaded nanoccarries spheres placed in a separate baker. The detailed preparation present in the corresponding table:

Table III.7. Sample Preparation Protocol for Drug Release Study.

N° tube	1	2	3
Volume of saline solution (ml)	10	10	10
The type of microsher drug – loed	oil	V_{B12}	Acid ascorbic

II.11.5. Application of drug – loaded nanospheres and the dressing from the medical side:

II.11.5.1. Application and efficacy of drug – loaded nanospheres : (under investigation)

the drug delivery beads, formulated from alginate polymer and nanoparticles synthesized using *rumex vesicarius* plant extract and loaded with mastic oil, are designed to treat colon cancer, this drug delivery system is characterized by its safe, natural composition and its ability to delivers the active compound directly to the effected colon cells, thereby enhancing therapeutic efficacy while minimizing side effects on healthy tissues. Furthermore, it effectively inhibits the growth of cancerous cells in the colon, making it a promising and innovative approach for colon cancer treatment.

II.11.5.2. Application and efficacy of the dressings:

The prepared dressing, based on alginate polymer and nanostructures synthesized from *haloxylon* SPP, enriched with mastic oil, is designed for the treatment of burns and wounds. It also exhibits antioxidant and antibacterial properties, as well as its ability to moisturize the affected area, thereby contributing to inflammation reduction and wound healing, ultimately restoring the integrity of body tissues.

Chapter III

Results and discussion

III.1. Introduction:

In this chapter, we present the results obtained through the experiments and analyses conducted within the framework of this work. We provided a detailed characterization of the synthesized nanoparticles using the green method, in order to understand their structure and behavior in the medium. The focus was placed on studying the physical, chemical and biological properties of the prepared sample, along with analyzing their response to experimental conditions. These results aim to evaluate the effectiveness of the developed nanocarrier system and determine its alignment with the previously defined objectives.

Iii.2. Characterization of nanoparticles and the prepared formalation:

Iii.2.1. Spectrophotometer uv – visible:

Iii.2.1.1. Silver nanoparticles ag nps :

During the verification teste for the formation of silver nanoparticles Ag NPs, it was initially abserved that solution exhibited a yellow color which gradually and after 15 min shifted to broun as the reaction progressed (indicate the formation of silver nanoparticles).

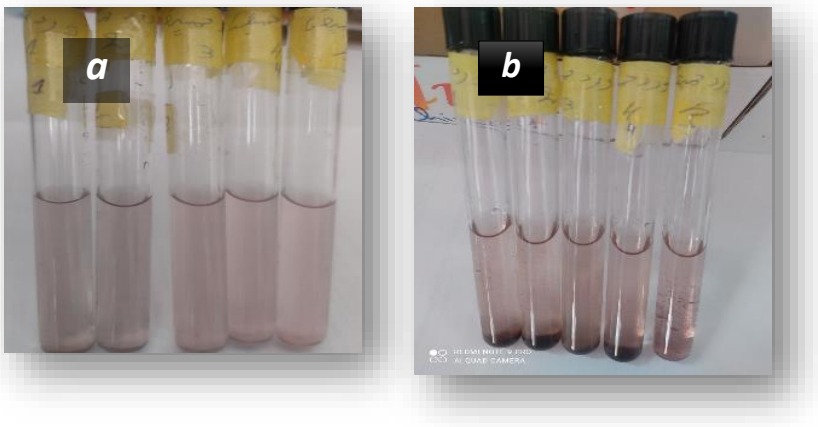


Fig III.1. samples of rumex extracte (a) drug preparation (b) after 15 min.

To confirm the formation of silver nanoparticles we use UV – visible spectrophotometer analyses in four samples prepared by mixing *Rumex vesicarius* extract with silver nitrate solution in different volum ration 1; 9,2; 8,3; 7 and 4;6 (extract: Ag NO_3). The results as showen in fig III.2. exhibited a characteristic absorbance peak at 341,05 nm in all samples, indicating the formation of Ag NPs. This peak corresponds to the surface Plasmon resonance (SPR) phenomenon. The highest absorbance was recorded at the 1; 9 ratio and gradually decreased with increasing extract proportion, suggesting that

the composition of the reaction medium influences the quantity and stability of the formed nanoparticles**[142].**

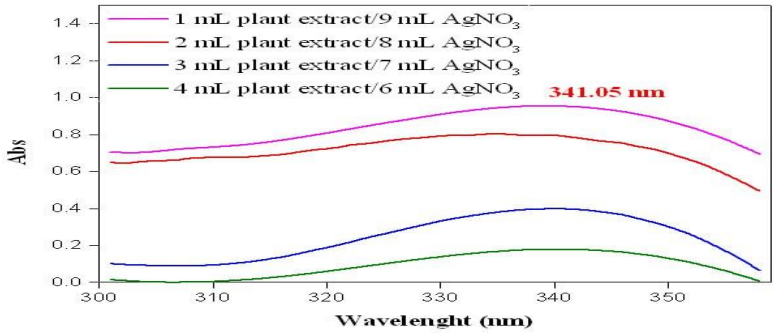


Fig III.2. UV – visible spectra of Ag NPs synthesized using *Rumex* extract.

III.2.. X- ray diffraction XRD:

Iii.2.2.1. Zinc oxide nanoparticles znonps :

X-ray diffraction (XRD) analysis was conducted to investigate the crystalline structure of zinc oxide nanoparticles (ZnO NPs) synthesized from different parts of the Rumex vesicarius plant, specifically the leaves and flowers. As shown in Figure III.1, both samples display characteristic diffraction patterns corresponding to hexagonal ZnO with a wurtzite crystal structure. These patterns match well with the standard Joint Committee on Powder Diffraction Standards (JCPDS) card No. 36-1451.

Prominent diffraction peaks were observed at 2θ values of approximately 31.7°, 34.4°, 36.2°, 47.5°, 56.6°, 62.9°, 66.4°, and 68.0°, which correspond to the (100), (002), (101), (102), (110), (103), (200), and (112) crystal planes, respectively. The sharpness and narrow width of these peaks indicate a high degree of crystallinity in the synthesized ZnO nanoparticles **[143].**

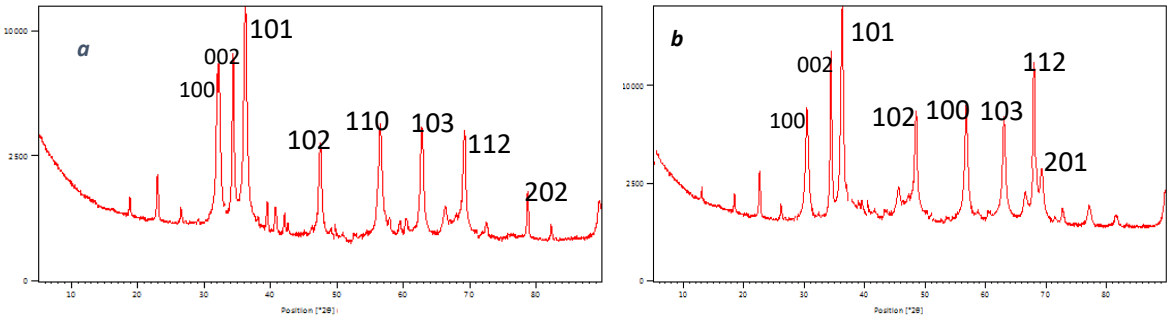


Fig III.3. *XRD pattern of the ZnO NPs sample extracted from the Rumex vesicarius plant. (a) from the leave (b) from the flower.*

- the particle size of the synthesized ZnO nanoparticles was estimated using the deby – Scherer equation and the results are presented in the table :

Scherrer equation ($D = K\lambda / \beta\cos\theta$) is used in XRD to calculate the crystallite size. In this equation, D is the average crystallite size, K is the Scherrer constant which is 0.68 to 2.08, 0.94 for spherical crystallites with cubic symmetry, λ is the X-ray wavelength, CuKα = 1.5406 angstrom, β is the line broadening at FWHM in radians, and θ is the Bragg's angle in degrees.

Table III. 1. XRD analysis data of ZnO nanoparticles of leaves and determination of their morphology in leave.

Parameters		Calculations				
K	**λ (Å)**	**Peak position 2θ (°)**	**FWHM β (°)**		**D (nm)**	**Average D (nm)**
0.94	**1.5406**	**32.63**	**0.65**	2.74	**13.30**	**16.03**
		34.82	**0.63**	2.57	**13.80**	
		36.28	**0.72**	2.47	**12.13**	
		47.53	**0.85**	1.91	**10.67**	
		56.52	**0.608**	1.62	**15.49**	
		62.84	**0.58**	1.47	**16.76**	
		79.12	**0.602**	1.20	**17.88**	
		78.72	**0.38**	1.21	**28.24**	

Table III.2. XRD analysis data of ZnO nanoparticles of flower and determination of their morphology in flower .

Parameters		Calculations				
K	**λ (Å)**	**Peak position 2θ (°)**	**FWHM β (°)**		**D (nm)**	**Average D (nm)**
0.94	**1.5406**	**30.845**	**0.57**	2.89	**15.10**	**20.19**
		34.42	**0.49**	2.60	**17.73**	
		36.18	**0.65**	2.48	**13.43**	
		48.54	**0.52**	1.87	**17.50**	
		56.38	**0.58**	1.63	**16.23**	
		62.92	**0.56**	1.47	**17.37**	
		67.94	**0.63**	1.37	**15.88**	
		77.22	**0.22**	1.23	**48.27**	

The average crystallite size of ZnO nanoparticles synthesized using *Rumex* leaf extract was found to be 16.03 nm, while those synthesized using Rumex flower extract showed an average size of 20.19 nm, confirming the nanometric nature of both samples.

The ZnO sample synthesized using the leaf extract exhibited peaks of higher intensity compared to the flower-derived sample. This suggests that the ZnO NPs formed from the leaf extract possess larger crystallite sizes and greater overall crystallinity.

In contrast, the ZnO sample synthesized from the flower extract exhibited a similar diffraction pattern in terms of peak positions (indicating a similar crystal phase), but with slightly lower peak intensities. These differences may be attributed to:

Smaller crystallite size

Increased lattice strain

Differences in the concentration and types of bioactive compounds (such as polyphenols, flavonoids, and organic acids) present in the flower extract, which can influence the nucleation and growth process of ZnO crystals.

These findings suggest that the part of the plant used for green synthesis can significantly influence the structural characteristics of the resulting ZnO nanoparticles. In particular, the leaf extract appears to promote the formation of more crystalline and possibly larger ZnO nanostructures, which could affect their physicochemical and functional properties in applications such as drug delivery or catalysis.

III.2.2.2. Silver nanoparticles Ag NPs :

The X – ray diffraction XRD pattern of the synthesized silver nanoparticles in figure III.4. displays and sharp diffraction peaks, confirming the crystalline nature of the AgNPs. The most intense peak is observed at approximately 2 $\theta \approx 38°$, which corresponds to the (111) plan of face – centered cubic (FCC) silver according to the standard JCPDS card No. 04-0783 **[144].**

Additional peaks located around 2 $\theta \approx 44{,}3°$, 64,5° and 77,4° are indexed to the (200 , 220 and 311) planes respectively, further confirning the FCC structure of metallic silver nanoparticles, where the broadening of the peaks, especially the 111 reflection suggests the nanometric size of the crystallites.

Scherrer's equation: $D = K\lambda/\beta\cos\theta$.

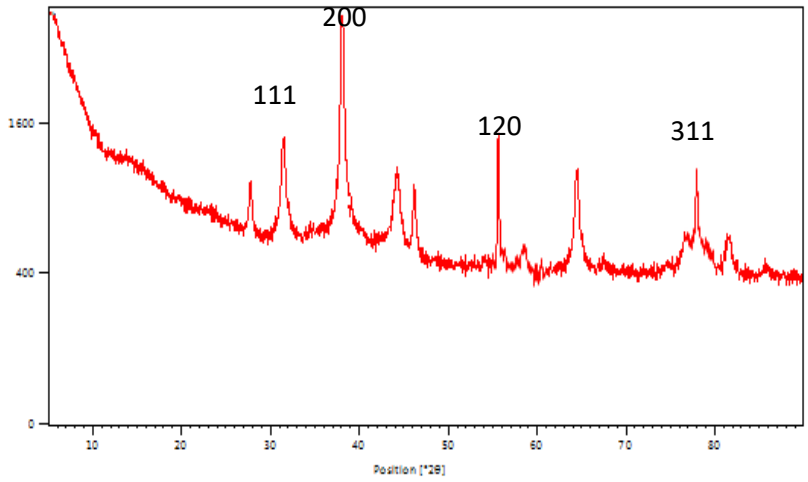


Fig III.4. XRD pattern of the Ag NPS.

Table III.3. XRD analysis data of Ag nanoparticles of flower and determination of their morphology using

Parameters			Calculations			
K	**λ (Å)**	**Peak position 2θ (°)**	**FWHM β (°)**		**D (nm)**	**Average D (nm)**
0.94	**1.5406**	**28**	**0.45**	3.18	**18.87**	**17.57**
		38.52	**0.57**	2.33	**15.32**	
		44.22	**0.68**	2.04	**13.13**	
		64.78	**0.49**	1.43	**19.97**	
		78.02	**0.52**	1.22	**20.54**	

The average crystallite size of biosynthesized silver nanoparticles (AgNPs) was calculated to be 17.57 nm, confirming the nanometric scale of all the prepared samples.

III.2.2.3. sphere laoded with ascorbic acid and V B12:

X – ray diffraction XRD analyses of ZnO beads loaded with ascorbic acid and vitamin B12 revealed a clear influence of active agents the crystalline structure. The ZnO / ascorbic acid bead retained the hexagonal (wurtizite structure), with distinct diffraction peaks observed at 2 θ = 31,7 , 34,4° , 36,2° ,47,5° ,56,6° ,62,8° and 67,9° **[120].**

Peak intensities were slightly reduced (1200 – 1600 units), likely due to surface coating by ascorbic acid. In contrast, the ZnO / vitamin B12 bead showed broader and weaker peaks (400 – 600 units) with a raised of an amorphous placed caused by structural interference from the larg molecular size of vitamin B12.

These results highlight that the nature of loaded bioactive compound directly affects the crystallinity of the ZnO nanostructures.

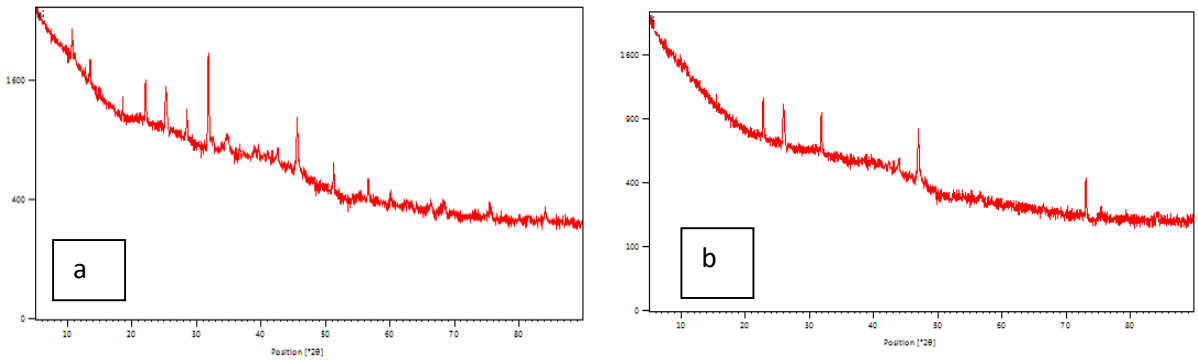


Fig III.5. *XRD analysis of the effect of ascorbic acid and vitamin B12 loading on the crystalline structure of ZnO NPs (a) zno of ascorbic acid (b)ZnO of vitaline B12.*

Iii.2.3. Scanning electron microscope sem:

Iii.2.3.1. Zinc oxide nanoparticles zno nps :

As shown in the attached SEM image Figure III.6, there is a clear difference in the morphology of zinc oxide nanoparticles synthesized from Rumex vesicarius leaf and flower extracts, ZnO leaves, nanoparticles, with an estimated size of 70 to 120 nm in contrast, ZnO flower exhibits more regular, three – dimensional flower – like structure, with a size of about 50 to 90nm. These values are estimated based on the image scale and the flower – like morphology provides a larger surface area,[148] which may enhance its effectiveness in nanomedical applications.

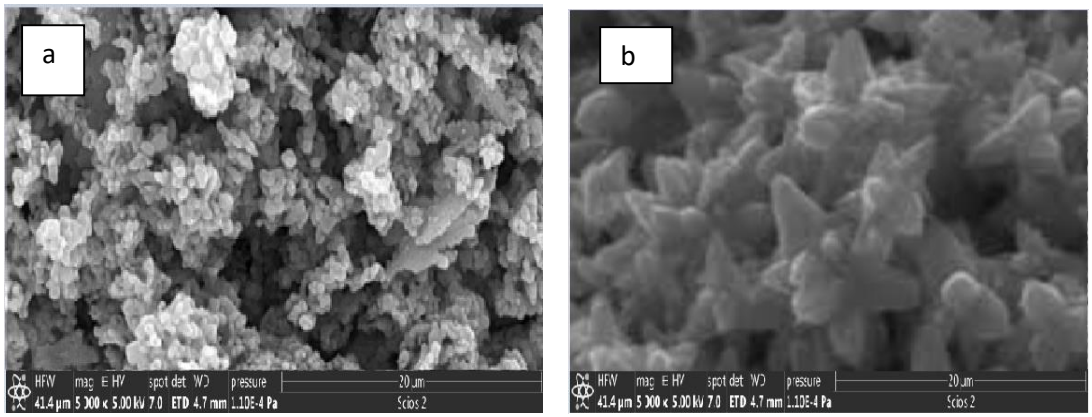


Fig III.6. *SEM image of ZnO NPs synthesized using (a) leaf of Rumex vesicarius ; (b)flower of Rumex vesicarius.*

Iii.2.3. Silver nanoparticles ag nps:

The SEM image of silver nanoparticles Ag NPs figure III.7. reveals a nanostructure with semi – spherical to flattened morphology, forming moderately dense aggregateds.

Based on the image scale (20 μm) and the appled magnification (X5300), the average between 80 and 150 nm. This relatively uniform distribution suggests a controlled crystalline grouth influenced by the biogenic reducing agent, indicating good particles stability **[145].**

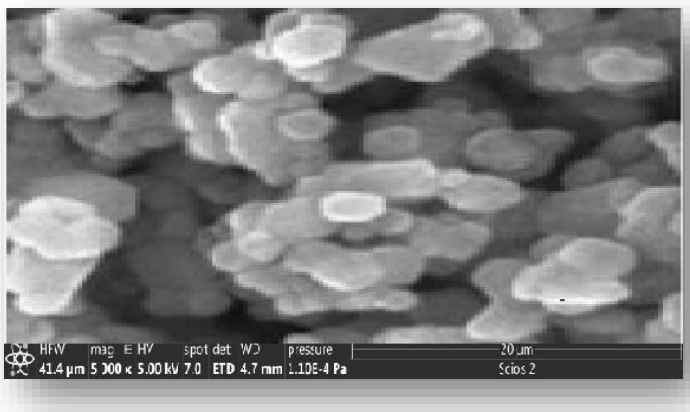


Fig III.7. *SEM image of green – synthesized silver nanoparticles .*

Thes morphological characteristics are promising for nanomedical applications, particularly as effective antimicrobial agents.

Iii.2.3.3. The sphere loaded with mastic oil:

The polymeric beads loaded with mastic oil analyzed using scanning electron microscopy SEM to evaluate their physical characteristics within a drug delivery system aimed at colon cancer treatment. The image Fig III.8.shows that the beads exhibit a relatively uniform spherical shape with a surface ranging from smooth to slightly rough, indicating good structural homogeneity and effective entrapment of the oil within the polymeric matrix based on the image, the bead diameters were estimated to range between 20 and 85 micrometers. These morphological features suggest a suitable structure for localized and sustained drug release **[120],** supporting their potential use as an efficient nanocarrier system for colon – targeted therapy.

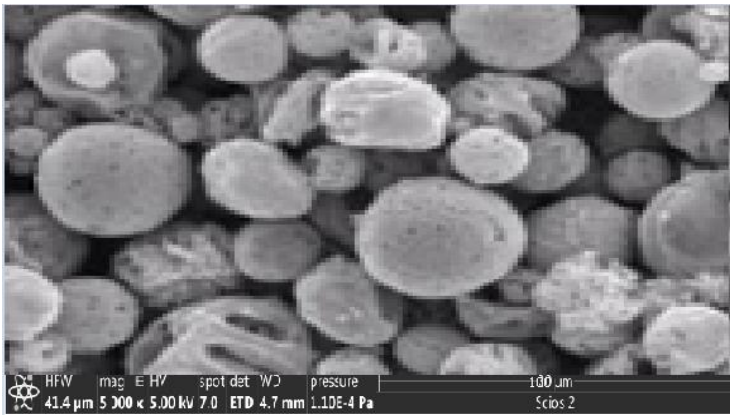


Fig III.8*. SEM image of the polymeric beads loaded with mastic oil .*

III.2.4. Microscopic characterization:

III.2.4.1. Microscopic characterization of the sphere loaded with mastic oil:

the synthesized sphere were examined using stereomicroscope. The observations revaluated that the sphere possess a generally spherical morphology with smooth and lustrous surfaces and coating a homogeneous outer matrix structure. The size distribrition appeared relatively uniform, reflecting a controlled and consistent fabrication process. The morphology suggest satisfactory physical integrity of the system and a potentially uniform dispersion of the encapsulated oil within the polymeric matrix.

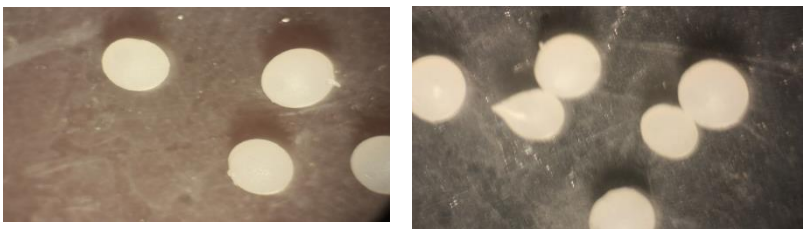


Fig III.9. *Microscopie images of the prepared sphere loaded with mastic oil under the stereomicroscope at different magnifications at X40 magnification .*

These morphological features were consistently observed a cross different magnification levels, further confirming the structural regularity of the prepared microparticles.

III.2.4.2. Microscopic characterization of the sphere leaded with vitamin B12:

the image fig iii.10 represents sphere loaded with vitamin B12, obtained using a stereomicroscope. The particles exhibit a nearly spherical shape with a smooth and transparent surface. Indicating a homogenous distribution of active ingredient within the polymeric matrix. This morphological uniformity reflects the successful loading technique and the physical stability of the prepared sphere.

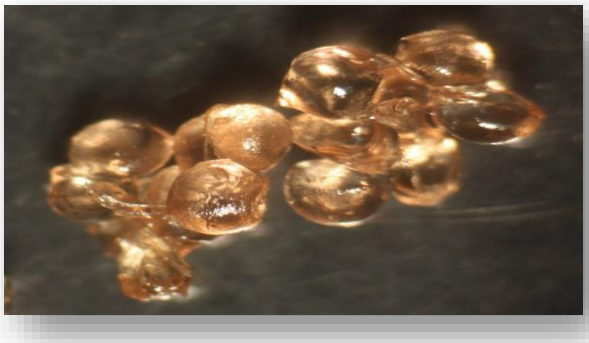


Fig III.10. *microscopie images of the prepared sphere loaded with vitamin B12 under the stereomicroscope at different magnifications at X40 magnification.*

III.2.4.3. Microscopic characterization of the ascorbic acid – loaded spheres:

The particles exhibit a semi – spherical structure with a transparent and slightly irregular surface, indicating a good distribution of the active compound within the polymeric matrix and confirming the efficiency of the loading technique and the physical stability of the prepared system.

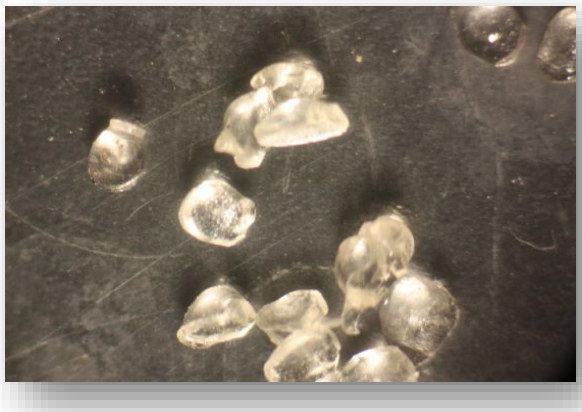


Fig III.11. *Microscopie images of the prepared sphere loaded with ascorbic acid under the stereomicroscope at different magnifications at X40 magnification.*

III.2.4.4. Microscopic characterization of alginate spher with nanoparticles:

The image (fig III.12) shows polymeric beads composed of alginate reinforced with nanoparticles (Ag NPs, ZnO NPs), without any active substance loading. The beads exhibit a semi – spherical shape with slight protrusions resulting from the gelation process. Their transparent stability and uniform distribution on the matrix components.

***Fig III.12**. Microscopie images of alginate sphere loaded with nanoparticles .*

III.3. Application tests:

III.3.1. Antioxidant tests :

III.3.1.1. Antioxidant activity of mastic oil, rumex vesicarius extracts and *haloxylon* SPP extract:

The antioxidant activity was evalited using the DPPH essay, which is based on the color change of the DPPH radical from purple to yellow in the presence of antioxidants. Ascorbic acide was used as standauded reference compound. The absorbance was measured at wavelength of 517 nm after one hour of reaction.

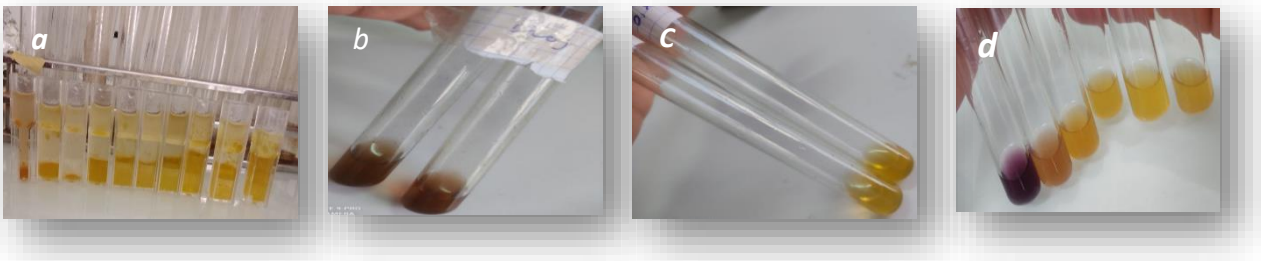


Fig III.13. Visual Observation of Sample Color Change After 1 Hour of Antioxidant Assay(a) Mastic oil(b) nanoparticuls (c)rumex flower (d) haloxylon.

- **Ascorbic acid :**

Ascorbic acid was used as a reference to evaluate antioxidant activity due to its high ability to scavenge free radicals. The two graphs illustrate absorbance and inhibition percentage as function of concentration the absorbance curve serves as baseline for calculating the antioxidant efficiency of the samples, while the inhibition curve highlights the strong antioxidant potential of ascorbic acid.

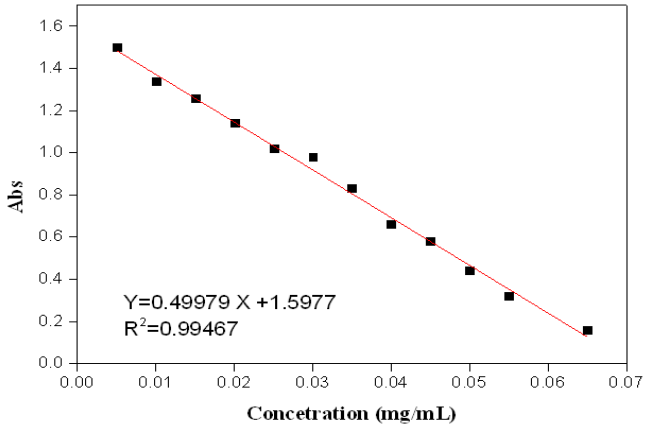


Fig III.14. Standard Curve of Ascorbic Acid for Antioxidant Assay A=f(c).

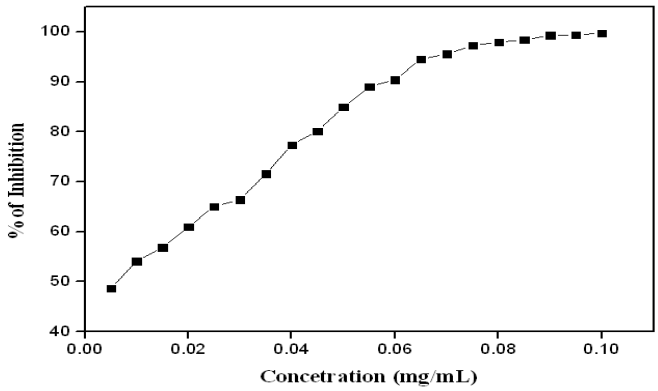


Fig III.15. Dose-Response Curve of Ascorbic Acid in Antioxidant Assay % inhibition=f (c).

- **Prepared and used materials:**

Based on the results of the antioxidant activity test using the DPPH method, figIII.16. illustrates the inhibition curves of rumex extract, haloxylon SPP extracts and mastic oil, where it is observed that the inhibition percentages increase with increasing concentration.

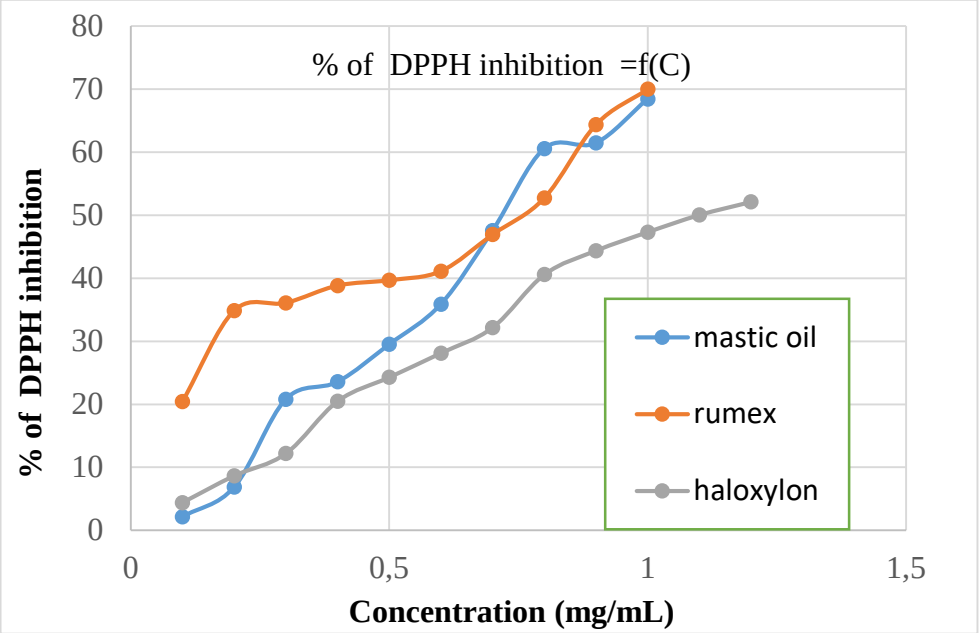


Fig III.16. DPPH Inhibition Curves of Mastic Oil, Rumex, and haloxylon Extracts.

To determine the amount of antioxidant equivalent to ascorbic acide, the IC_{50} value was determined and the concentration of antioxidant in the prepared samples relative to ascorbic acide was calculated at the highest percentages (highest % $\Leftrightarrow c = 1mg/ml$)the results were presented in a table and corresponding bar charts.

Table III.4. antioxidant activity paramaters at IC_{50} :

samples	**Ascorbic acide**	***Rumex* extract**	***Haloxylon* extract**	***Mastic oil***
IC_{50} (mg/ml)	0,0065	0,76	1,1	0,71

Table III.5. antioxidant activityvalues based on DPPH essay in C=1mg/ml samples:

samples	*Mastic oil*	*Rumex* extracts	*Haloxylon* extracts	ZnO NPs (flower)	ZnO NPs (Leveas)	ZnO NPs (Haloxylon)	Ag NPs (Flower)
Highest inhibition%	68,46	70	47,33	92,78	91,9	90,5	91?29
Highest absorbance A max	0,92	0,87	1,54	0,21079	0,2353	0,2771	0,2544
C(mg ascorbic acide/ml)	1,88	1,77	3,14	0,4	0,48	0,57	0,51

R.vesicarius extract showed the highest antioxidant activity (1,77 – 70 %) flower by mastic oil (1,88 – 68,46 %) and *haloxylon* SPP extract (3,14 – 47,33)% , aliging with IC $_{50}$ rankings. Among nanomaterials, zinc oxide nanoparticles from Rumex flower showed highest activity, followed by these leaves and haloxylon. silver nanoparticles from Rumex flower also exhibited strong inhibition (91,29%). These comparative rations are illustrated in the bar charts .

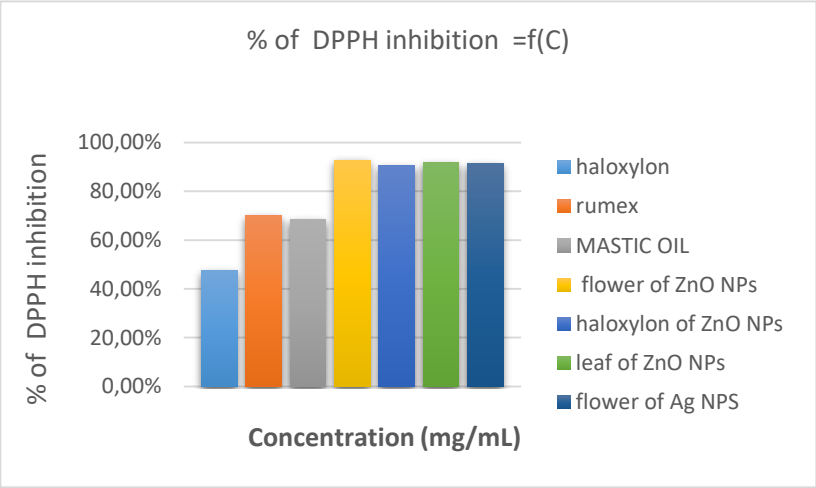


Fig III.17. bar chart of inhibition percentage for test samples in C=1mg /ml samples.

Result :

- ✓ *Rumex vesicarus* extract showed the highest antioxidant content among the tested samples, allowing it to be classified as potent natural antioxidant **[128].**
- ✓ Ascorbic acide exhibited the strongest antioxidant activity due to its high purity, making it significantly more effective than Rumex vesicarius, haloxylon SPP, mastic oil and the nanoparticles.
- ✓ Some nanoparticles demonstrated antioxidant activity close to that of ascorbic acide, indicating their promising potential in drug delivery systemes and wound – healing applications.

III.3.2. Release teste:

The release of active compounds (mastic oil , ascorbic acid, vitamin B12) from the spheres was evaluated using the DPPH essay by measuring antioxidant activity over 50 min.

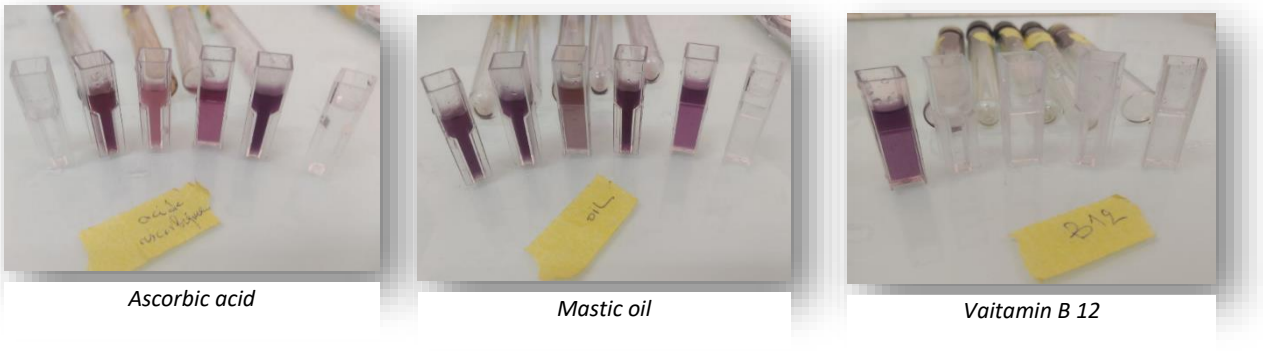
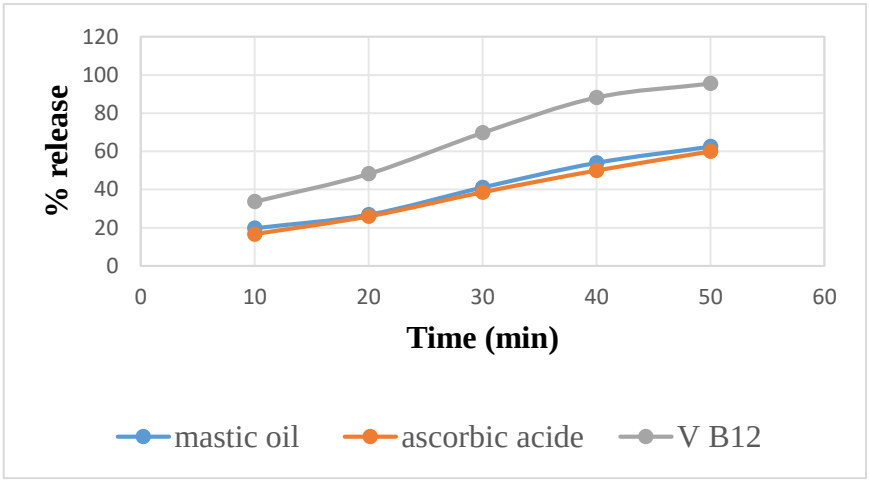


Fig III.18. Visual Observation of Sample Release After 1 Hour.

The absorbance was recovded at 517 nm using UV – visible spectrophotometer, the inhibition rates were calculated based on the measured absorbance and a time – dependent curve was plotted to monitor the releaseof the active compounds.



FigIII.19*. kinetic profile of active compound release under simulated conditions.*

Table III.6. Summary Table of Antioxidant Activity Calculations.

Release profile data	Sphere of Mastic oil	Sphere of V B12	Sphere of ascorbic acide
Inatial inhibition%	19,69	33m63	16,57
Inhibition persontag oven tme	[20 - 30]		
Time to reach maximum inhibition min	At the 50 th min		
Maximum inhibition	62,47	95,55	60

Based on the release curve, a progressive increase in the inhibition percentage was observed for mastic oil, rising from 19.69% to 62.47% over the duration of the experiment. This pattern indicates a sustained and controlled release of the bioactive compound, which is essential for maintaining prolonged therapeutic activity. The gradual release is particularly beneficial for applications requiring extended antioxidant or antimicrobial protection, such as in skin creams or wound-healing formulations.

For ascorbic acid (vitamin C) and vitamin B12, the release profiles were similar at the initial stage; however, vitamin B12 showed a rapid and almost complete release within a shorter timeframe. This may be attributed to the higher solubility and lower molecular weight of vitamin B12, allowing it to diffuse more easily from the alginate matrix. In contrast, ascorbic acid exhibited a moderately controlled release, potentially due to stronger interactions with the carrier matrix or differences in encapsulation efficiency.

These differences in release kinetics reflect the distinct physicochemical properties of each active compound:

Mastic oil, being hydrophobic, is retained longer within the hydrophilic alginate network, leading to slower diffusion.

Vitamin B12, a water-soluble molecule, diffuses rapidly once the matrix is hydrated.

Ascorbic acid, while also water-soluble, may interact more with the matrix, slowing its release relative to vitamin B12.

The release data strongly support the efficacy of the formulated drug delivery system, confirming its ability to control and modulate the release of encapsulated compounds. The sustained release of mastic oil suggests the system is well-suited for long-acting applications, while the rapid release of vitamin B12 may be ideal for immediate therapeutic action when quick absorption is required.

Overall, these findings demonstrate that the prepared microspheres act as intelligent delivery vehicles, capable of tuning the release profile based on the encapsulated compound’s properties. This provides a versatile platform for cosmetic and pharmaceutical applications, including antioxidant therapy, anti-aging products, and targeted drug delivery.

General conclusion

GENERAL CONCLUSION

This thesis falls within the framework of developing innovative nanomedical systems for therapeutic purposes using nanotechnology. During the study, nanostructures were prepared by integrating alginate polymer with active natural substances such as *mastic oil* and other plant extracts. Environmentally friendly preparation methods were adopted, specifically green synthesis, which aims to combine the benefits of nanotechnology with the therapeutic efficacy of medicinal plants. In the context of designing targeted drug delivery systems for the treatment of complex diseases, *rumex vesicarius* was used to fabricate drug carriers loaded with mastic oil for the treatment of colon cancer. Additionally, *haloxylon* SPP was utilised to develop wound dressings intended to accelerate burn healing and wound closure.The methodology focused on the fabrication of a nanostructured formulation with enhanced physicochemical properties using silver nanoparticles (Ag NPs) and zinc oxide nanoparticles (ZnO NPs), while relying on advanced analytical techniques for the characterisation of the particles, including scanning electron microscopy (SEM) and X-ray diffraction (XRD), in addition to analyses of the extracts and oil. Ultraviolet-visible spectroscopy (UV-Vis) zinc oxide is characterised by its antioxidant properties and contributes to the stability of nanocarriers and the targeting of cancer cells. Silver nanoparticles are known for their antibacterial and anti-inflammatory activities, in addition to their potential effects on cancer and tumour cells, supporting their use in the treatment of cancer and burns.The results revealed that XRD analysis confirmed that ZnO NPs and Ag NPs were crystalline and well-structured, with ZnO NPs showing a hexagonal (wurtzite) and silver a cubic structure. Spheres loaded with vitamin B12 and ascorbic acid exhibited altered peak intensities and increased background, indicating successful loading and reduced crystallinity. SEM images showed ZnO NPs were spherical and compact, averaging [82 – 102] nm in size, while beads loaded with mastic oil for colon cancer treatment displayed a smooth, homogenous morphology, reflecting effective encapsulation and good stability. Microscopic observations confirmed structural regularity with slight variations depending on the active compound. UV-vis analysis confirmed that Ag NPs were successfully made from rumex flower extract, which showed strong antioxidant activity. Some green – synthesised nanoparticles also showed antioxidant potential comparable to ascorbic acid, supporting their biomedical relevance in drug delivery and wound healing. The release profile of the active compound was controlled and gradual, confirming the carrier's efficiency in sustained and targeted delivery.

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