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Nanotechnology in herbal medicine

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Ilham and Hadjer

Dedications

*Name of Allah, the Most Gracious, the Most Merciful. All praise is due to Allah, by whose grace good deeds are completed, by whose favor goals are attained, and by whose guidance difficulties are overcome. After an academic journey spanning years—marked by **challenges, lessons, and tireless effort**—I now stand at the threshold of graduation, carrying in my heart profound gratitude. With these words, I pen this dedication as a humble token of appreciation to everyone who played a role in this achievement.*

***In cherished memory of my late mother, Salima,** who was my first support. Though physically absent, her pure soul and prayers remain my constant guide, instilling in me a love for knowledge, patience, and diligence. I dedicate the fruits of my efforts to her, acknowledging that without her prayers, this moment wouldn't be possible.*

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***To my beloved family,** the perpetual light on my path. My heartfelt thanks extend to my **grandmother**, whose sincere prayers guided me, and my **aunt**, a constant source of warmth and compassion. To my dear **siblings: Nawari, Sabrina, Rima, Ridha, Amir, and Maram**—you are my joy and strength. This work is a testament to your collective love and support, which sustained me through every challenge and brought joy to every accomplishment.*

***To my dear friends, Samah and Maysaa,** who were more than friends; you were sisters and unwavering support through every stage of this journey.*

And finally...

To my self

You were strong, patient, and determined. You made it — and you deserve every bit of this success.

Moussaoui Hadjer

Dedications

*Name of Allah, the Most Gracious, the Most Merciful. All praise is due to Allah, by whose grace good deeds are completed, by whose favor goals are attained, and by whose guidance difficulties are overcome. After an academic journey spanning years—marked by **challenges, lessons, and tireless effort**—I now stand at the threshold of graduation, carrying in my heart profound gratitude. With these words, I pen this dedication as a humble token of appreciation to everyone who played a role in this achievement.*

*To the soul of my beloved father **Massoude**,Though you're no longer in this world, your love and prayers continue to guide me.This achievement is for you — may it reach your soul and make you proud.*

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Your sacrifices built the path I walk today. Thank you for everything — I owe this to you.

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You were my rock, my quiet strength, always there without needing to be asked.
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You brought light to my hardest days and joy to my journey. I'm grateful for each of you.

And finally...

To my self

You were strong, patient, and determined. You made it — and you deserve every bit of this success.

Abdiche Ilham

Abstract

Nanotechnology is a multidisciplinary scientific field that has significantly transformed various sectors, especially biomedical and life sciences. It has proven effective in enhancing drug properties by improving bioavailability, controlled release, and targeted delivery. Recently, growing interest has emerged in integrating nanotechnology with herbal medicine, as it offers solutions to challenges associated with phytochemicals, such as poor stability and limited absorption. This approach involves the green synthesis of nanoparticles using plant extracts a sustainable, eco-friendly method that combines the therapeutic potential of natural compounds with the unique physicochemical characteristics of nanomaterials.

The nanoparticles synthesized via this green route have demonstrated promising biological properties, including antimicrobial, antioxidant, and cytotoxic activities. These particles were characterized using analytical techniques such as UV-Vis spectroscopy, FTIR, SEM, among others. The use of plant-based nanoparticles highlights an effective scientific convergence between advanced nanotechnology and traditional herbal medicine, paving the way for the development of innovative therapeutic systems that are safer, more effective, and environmentally sustainable. This reinforces the potential of nanophytomedicine as a growing field in both research and clinical applications.

Keywords: Nanotechnology, green synthesis, nanoparticles, herbal medicine, biological activities.

Résumé

La nanotechnologie est un domaine scientifique multidisciplinaire qui a profondément transformé plusieurs secteurs, en particulier les sciences biomédicales et biologiques. Elle a démontré son efficacité dans l'amélioration des propriétés des médicaments, notamment en augmentant leur biodisponibilité, en permettant une libération contrôlée et un ciblage précis. Ces dernières années, un intérêt croissant s'est manifesté pour l'intégration de la nanotechnologie à la médecine par les plantes, en raison de son potentiel à surmonter les limitations des composés photochimiques, tels que leur faible stabilité et leur absorption limitée.

Cette approche repose sur la synthèse verte des nanoparticules à partir d'extraits végétaux, une méthode écologique et durable qui associe le pouvoir thérapeutique des plantes aux propriétés physico-chimiques uniques des nanomatériaux. Les nanoparticules obtenues par cette méthode ont montré des activités biologiques prometteuses, notamment antimicrobiennes, antioxydants et cytotoxiques. Leur caractérisation a été réalisée à l'aide de techniques analytiques telles que la spectroscopie UV-Vis, la FTIR et la microscopie électronique à balayage (MEB), entre autres.

L'exploitation de ces nanoparticules d'origine végétale met en évidence une convergence scientifique pertinente entre nanotechnologie avancée et médecine traditionnelle, ouvrant la voie à la mise au point de systèmes thérapeutiques innovants, plus sûrs, plus efficaces et respectueux de l'environnement. Ce travail souligne ainsi le potentiel de la nanophytomédecine comme champ émergent dans la recherche biomédicale et les applications cliniques.

Mots-clés : Nanotechnologie, synthèse verte, nanoparticules, phytothérapie, activités biologiques.

الملخص

تُعد تقنية النانو مجالًا علميًا متعدد التخصصات، ساهم بشكل كبير في إحداث نقلة نوعية في العديد من القطاعات، لا سيما في التطبيقات الطبية والبيولوجية. وقد أثبتت هذه التقنية فعاليتها في تحسين خصائص الأدوية من خلال تعزيز التوافر الحيوي، والتحكم في إطلاق المادة الفعالة، وتحقيق استهداف دقيق للخلايا. وفي هذا السياق، برز اهتمام متزايد بتكامل تقنية النانو مع الطب النباتي، لما تقدمه من حلول لتجاوز العقبات المتعلقة بالمركبات النباتية، مثل ضعف الثبات الكيميائي وصعوبة الامتصاص.

يعتمد هذا التوجه على التخليق الأخضر للجسيمات النانوية باستخدام مستخلصات نباتية، وهو نهج صديق للبيئة يجمع بين الفعالية العلاجية الطبيعية للنباتات والخصائص الفيزيوكيميائية الفريدة للمواد النانوية. وقد أظهرت الجسيمات الناتجة خصائص بيولوجية واعدة، شملت النشاط المضاد للميكروبات، والقدرة المضادة للأكسدة، والنشاط السمي الخلوي ضد بعض الخلايا السرطانية. وتم توصيف هذه الجسيمات باستخدام تقنيات تحليلية دقيقة مثلUV-Vis ، FTIR، وSEM، وغيرها. إن استخدام الجسيمات النانوية ذات الأصل النباتي يُظهر تكاملًا علميًا فعّالًا بين التكنولوجيا المتقدمة والطب التقليدي، مما يمهّد الطريق لتطوير أنظمة علاجية مبتكرة تتميز بالأمان والفعالية والاستدامة البيئية. وهو ما يعزز من مكانة الطب النانوي النباتي كمجال واعد في البحث والتطبيقات السريرية المستقبلية.

الكلمات المفتاحية: تقنية النانو، التخليق الأخضر؛ الجسيمات النانوية، طب الاعشاب، النشاط البيولوجي.

List of abbreviations

AES: Auger Electron Spectroscopy

AFM: Atomic Force Microscopy

AgNPs: Silver Nanoparticles.

AuNPs: Gold Nanoparticles

CMAR: Carcinogenic Mutagenic Asthmagenic Reproductive

CuNPS: Cupper nanoparticles

DLS: Dynamic Light Scattering

EDS: Energy-Dispersive X-ray Spectroscopy

FTIR: Fourier Transform Infrared Spectroscopy.

LEIS: Low-Energy Ion Scattering

Me: Metal ion

MnO_2 NPs: Manganese Dioxide Nanoparticles

MNPs: Metal Nanoparticles

NMs: Nanomaterials

NNI: National nanotechnology initiative

NPs: Nanoparticles

RNA: Ribonucleic Acid

ROS: Reactive Oxygen Species

SEM: Scanning Electron Microscopy

SiO_2 NPs: Silicon dioxide nanoparticles

SLN: Solid lipide nanoparticul

SOD: Superoxide Dismutase.

SPM: Scanning Probe Microscopy

SPR: Surface Plasmon Resonance

STM: Scanning Tunneling Microscopy

TEM: Transmission Electron Microscopy

TiO_2 NPs: Titanium Oxide nanoparticles

ToF SIMS: Time-of-Flight Secondary Ion Mass Spectrometry**.**

XPS: X-ray Photoelectron Spectroscopy

XRD: X-ray diffraction

ZnO NPs: Zinc Oxide nanoparticles

ZP: Zeta Potential

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Introduction

Introduction

Interest in nanomaterials and especially nanoparticles has exploded in the past decades primarily due to their novel or enhanced physical and chemical properties compared to bulk material. These extraordinary properties have incorporated into almost every domain of science and technology and created a multitude of innovative applications in the fields of medicine and pharma, electronics, agriculture, food industry, and many others (Joudeh & Linke, 2022). Nanotechnology possesses a prospect to significantly bestow major environmental and health advantages (Hoy et al., 2021).

Plants and herbal medicines have been used for medicinal purposes since ancient times due to their broad public acceptance, affordability, minimal side effects, safety and cost-effectiveness compared to conventional drugs. They contain phytochemicals natural compounds known as secondary metabolites that offer various pharmacological benefits. However, their effectiveness is often limited various factors (Dewi et al., 2022). Nanotechnology offers a solution to these challenges by the integration of herbal drugs into nanomatrix systems using nanoparticles. This innovative approach gained global renewed interest in developing advanced, nanotechnology-based herbal formulations and enhancing therapeutic potential (Dewi et al., 2022; Kalita et al., 2023).

Nanotechnology is a process that combines the basic attributes of biological, physical, and chemical sciences. Physically, the size is reduced; chemically, new bonds and chemical properties are governed (Malik et al., 2023). More recently, nanoparticles are also being synthesized biologically through the use of plant- mediated processes, as an environmentally friendly alternative compared to toxic physical and chemical synthesis methods (Joudeh & Linke., 2022). This transdisciplinary approach to nanoparticle synthesis requires that biologists and biotechnologists understand and learn to use the complex methodology needed to properly characterize these processes (Joudeh & Linke., 2022). Several techniques have been used to characterize the size, crystal structure, elemental composition and a variety of other physical properties of nanoparticles (Mourdikoudis et al., 2018).

In this research, we summarize a comprehensive overview of the different classes of nanoparticles, their applications, phytosynthesis, characterization analysis, certain biological activities and their enhanced benefits given for herbal medicines, which help to limit their inconvenient in drug delivery system and help also to develop a sustainable agriculture. In this context, this research are given by three parts:

- The first part of this work, we have focused on nanoparticles, their classification and its uses in various fields including their application in the fields of medicine, energy and food fields.

- The second one focus on herbal medicine and address how nanotechnology will be integrated into herbal medicine.

- Finally, the third part focus on the nanomaterials phytosynthesis by medicinals plants, the characterization techniques and certain therapeutic use of them.

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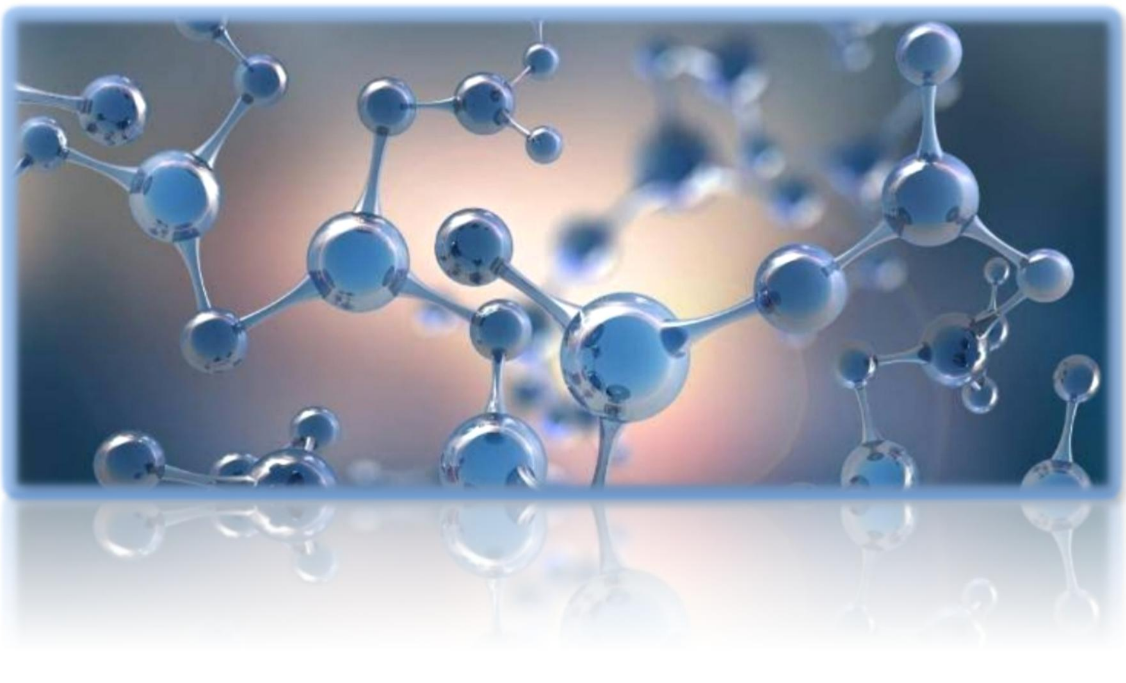
Chapter I
Nanotechnology



I. Nanotechnology

I.1. Generality

The prefix “nano” comes from the Greek word meaning, “dwarf” or something extremely small, it’s important to distinguish between nanoscience and nanotechnology. Nanoscience is the study of structures and molecules at the nanoscale typically between 1 and 100 nanometers (nm) (Bayda et al., 2019). Nanotechnology is the science of manipulating atoms and molecules to alter the chemical and physical properties of materials (Barhoum et al., 2022).

In short, nanotechnology is the ability to construct materials and products both micro and macro in a way that achieves atomic-level precision. The true promise and essence of nanoscale science and technology lie in the fact that materials at the nanoscale exhibit unique properties chemical, electrical, magnetic, mechanical, and optical that differ significantly from their bulk counterparts.

For example, opaque materials like copper can become transparent, inert elements such as platinum can act as catalysts, stable substances like aluminum may become combustible, solid metals like gold can turn into liquids at room temperature, and insulating materials such as silicon can behave as a conductor (Singh et al., 2023).Nanotechnology holds significant importance in various scientific and technological advancements (Khan et al., 2022).

I.2. History

Nanotechnology has existed since ancient times and has witnessed significant development over time in several stages. The evolution of nanotechnology began in 1857(Barhoum et al., 2022), and its key developmental milestones are summarized in Table I.

Table I: Timeline of nanomaterial discovery in the modern nanotechnology era (Barhoum et al., 2022).

Year	Development in Nanotechnology
1857	Michael Faraday studied the fabrication and properties of "Ruby" gold colloidal suspensions.
1905	Estimated the size of a sugar compound to 1 nm.
1935	Development of the first electron microscope.
1952	First observation of carbon nanotubes.
1959	Richard Feynman gave the first nanotechnology talk: *"There's Plenty of Room at the Bottom."*
1981	Invention of the Scanning Tunneling Microscope.
1981	The term "nanotechnology" was first introduced by Norio Taniguchi.
1985–1987	Popularization through *Engines of Creation*, fullerene discovery, Foresight Institute founded.
1990	First issue of the journal *Nanotechnology*.
1991	Elucidation of carbon nanotube structure.
1997–1999	Development of nanowire circuit at HP, first nanoswitch, National Science Foundation inter-agency, nanotube transistor.
2000	Launch of the national nanotechnology initiative (NNI), first PhD program in nano, International Business Machines-Delft transistor.
2003	21st century nanotechnology Research and Development Act passed; Greenpeace issued public memoranda.
2004	Rediscovery of graphene; insurance companies began risk assessments for nanoproducts.
2007	$1.4 billion in funding allocated for the NNI.
2009	Development of NPs for *in vivo* drug delivery.
2016	Studies on the environmental and biological toxicity of Nanoparticle.

I.3. Nanomaterials

I.3.1. Definition

NMs are particles with dimensions on the nanometer scale in all three spatial directions (Mirsasaani&Arshadi Poshtiri, 2019). The term Nps encompasses both nanocapsules and nanospheres, which differ primarily in their morphological structure (Zielińska et al., 2020). The comprehensive definition of Nps typically falls within the domain of physical chemistry, as their behavior is influenced not only by directly measurable quantities such as mass, volume, and electric charge, but also by their inherent ability to self-organize due to high surface reactivity.

Nanoparticles (NPs) are of significant scientific interest because they serve as an intermediate state between bulk materials and atomic or molecular structures. Unlike bulk substances, which exhibit consistent physical and chemical properties regardless of size, NPs display size-dependent behaviours governed by discrete molecular or atomic phenomena (Strambeanu et al., 2015). The (Figure1) indicated the comparing the sizes of Nps with to those of larger- scale materials.

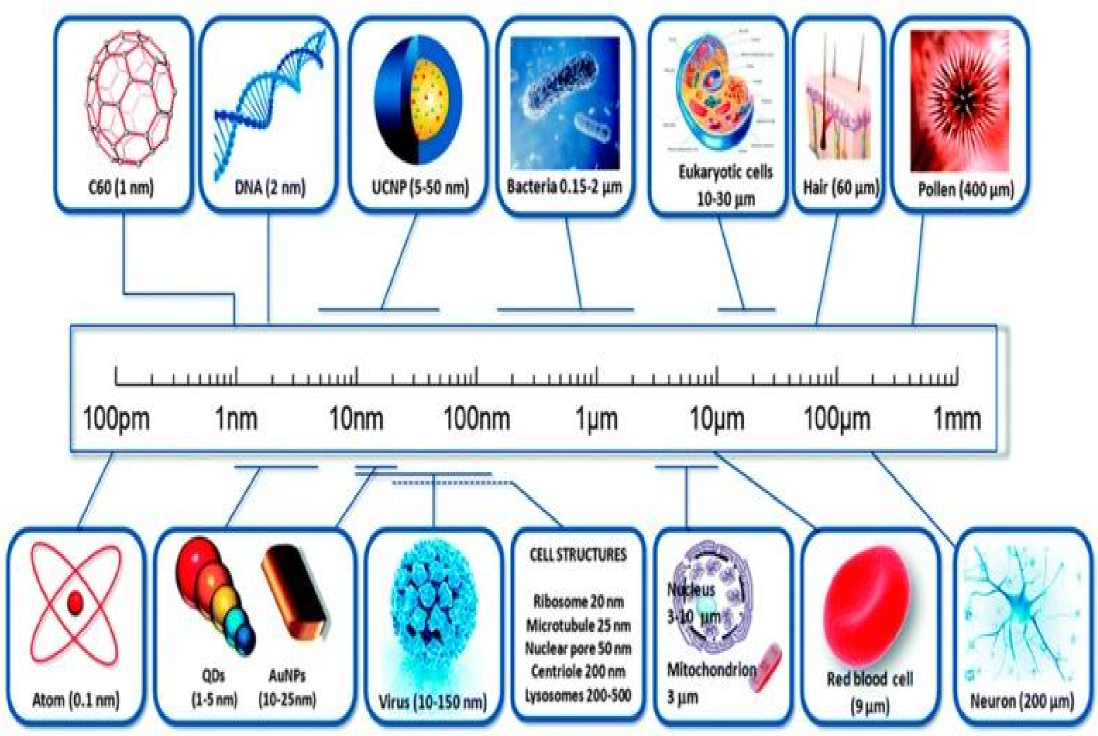


Figure 1: Comparing the sizes of nanomaterials (NMs) (Bayda et al., 2019).

I.3.2. Classification

NMs are broadly classified into various categories (Figure 2) based on origin, their structural configuration, number of dimensions, pore of dimension, based and potential toxicity (Mekuye & Abera, 2023).

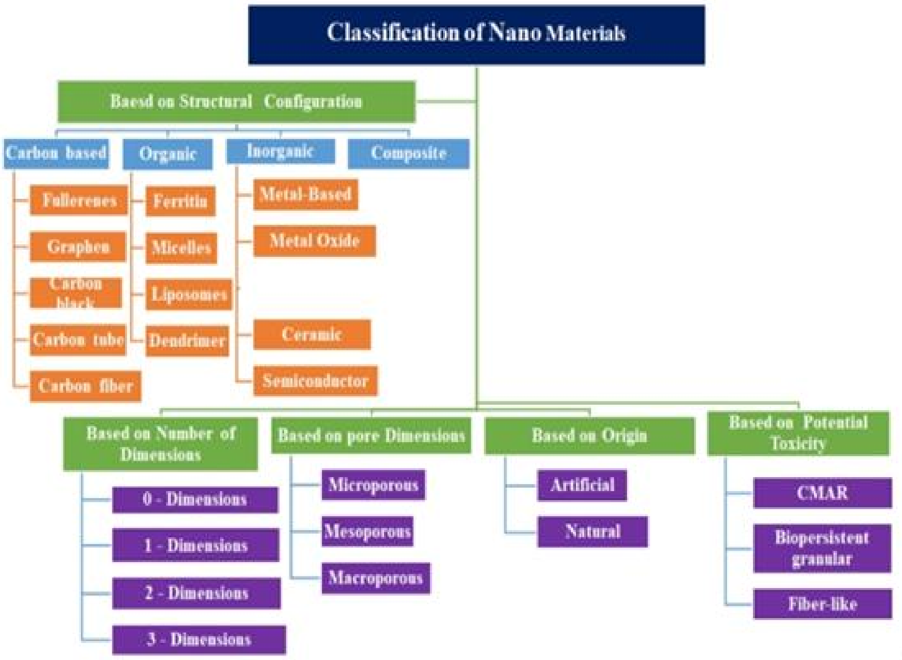


Figure 2: Classification of NMs (Mekuye & Abera, 2023).

I.3.2.1. Based on origin

Natural and artificial NPs (Figure 3) are the two groups into which NMs are divided based on origin (Mekuye and Abera, 2023).

Figure 3: Classification of NPs based on origin type (personal image)

I.3.2.1.1. Natural NPs

In nature, natural NMs can be produced either by living organisms or through human activities. Regardless of human influence, NMs are naturally present across all spheres of the Universe such as the hydrosphere, atmosphere, lithosphere, and biosphere. Examples of NMs found in Earth's systems include those in the hydrosphere, which consists of seas, lakes, rivers, groundwater, and hydrothermal vents; the lithosphere, which contains rocks, soils, magma, and lava during certain geological stages; and the biosphere, which encompasses both lower and higher life forms, including humans and microorganisms (Singh et al., 2023).

Table II lists various natural NMs present in some living organisms such as human body and microorganisms.

Table II: Natural NMs in living organisms (Barhoum et al., 2022).

Occurrence	Nanostructure	Thickness/Diameter (nm)
Human body	DNA	2-2.5nm
	Enzymes	3-7nm
	Antibodies	10-15nm
	Bone collagen fibrils	60-70nm
	Mitochondria	1000nm
Microorganisms	Bacteria	0.6-5000 nm
	Virus	50-150 nm
	Fungi	Setae with a spatula of 50-100 nm in size

I.3.2.1.2. Artificial NPs

Synthetic (engineered) NMs can be produced through physical, chemical, biological, or hybrid methods, as well as by mechanical grinding, engine emissions, and smoke (Singh et al., 2023). Engineered nanomaterials are produced to meet specific requirements, such as nanostructured medical implants. These NPs typically exhibit uniform shapes and sizes, including rings, fullerenes, carbon nanotubes, spheres, and graphene (Harish et al., 2022).

I.3.2.2. Based on structural configuration

Based on their composition, NPs are generally placed into three classes: organic, carbon-based, and inorganic (Joudeh & Linke, 2022).

I.3.2.2.1. Carbon-based NPs

Fullerenes, Graphen, carbon black, carbon fiber and carbon nanotubes (Figure 4) represent four key subcategories of carbon-based Nps (Mekuye & Abera, 2023).

- **Fullerenes**

Fullerenes consist of globular, hollow cage-like structures composed of carbon allotropes. Their unique properties such as high electrical conductivity, mechanical strength, electron affinity, and structural adaptability have generated considerable economic and scientific interest. These molecules are composed of organized pentagonal and hexagonal carbon units (Altammar, 2023).

- **Graphen and Graphene oxide**

Graphene enhances polymer-based nanocomposites due to its excellent mechanical, electrical, and barrier properties. However, pure graphene has drawbacks like difficult synthesis, low solubility, and agglomeration. Graphene oxide, produced via a simpler top-down method, offers a practical alternative with better solubility and easier surface modification. Graphene oxide disperses well in polymers, forms dense structures that block gases, and is widely used in packaging, electronics protection, and corrosion resistance. Its unique properties also make it useful for stimuli-responsive materials (Khan et al., 2022).

- **Carbon black**

An amorphous carbon-based material with diameters typically between 20 and 70 nm, often spherical in shape. The particles interact strongly, causing them to form agglomerates approximately 500 nm in size (Sune et al., 2024).

- **Carbon fiber**

Carbon nanofibers are made from the same graphene nanofoils as carbon nanotubes, but instead of forming standard cylindrical tubes, they are twisted into cone or cup shapes (Sune et al., 2024).

- **Carbone nanotube**

Carbon nanotubes elongated tubular structures with diameters typically ranging from 1 to 2 nm. Structurally, they can be envisioned as rolled sheets of graphene, and are categorized based on the number of layers or walls they possess. These include single-walled, double-walled, and multi-walled carbon nanotubes (Altammar, 2023).

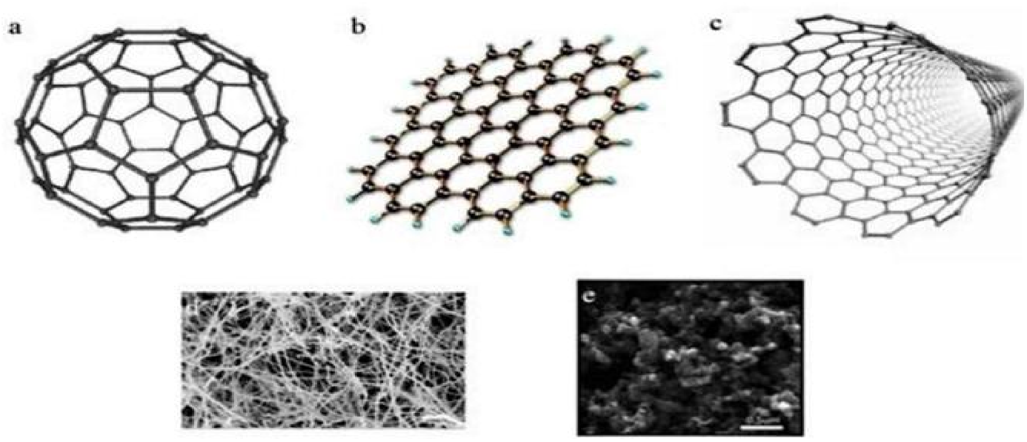


Figure 4: Carbon based nanoparticles: a) fullerenes, b) graphene, c) carbon nanotubes, d) carbon Nanofibers and e) carbon black (Sune et al ., 2024).

I.3.2.2.2. Organic NPs

Organic NPs are derived from natural or synthetic organic molecules (Mekuye & Abera, 2023). Nature offers numerous examples of organic NPs, including protein aggregates, lipid bodies, milk emulsions, and more complex organized structures such as viruses (Romero & Moya, 2012). Some examples of these NPs are lipid-based NPs, which are generally spherical, with diameters ranging between 10 and 100 nm. Lipid-based NPs systems (Figure 5) consisting of vesicular systems (liposomes), lipid NPs , and nanoemulsions (Lokole et al., 2024). It consists of a solid core made of lipids and a matrix containing soluble lipophilic molecules (Mekuye & Abera, 2023). They are capable of encapsulating a wide range of therapeutic agents, including small molecules, nucleic acids, and monoclonal antibodies (Mehta et al., 2023).

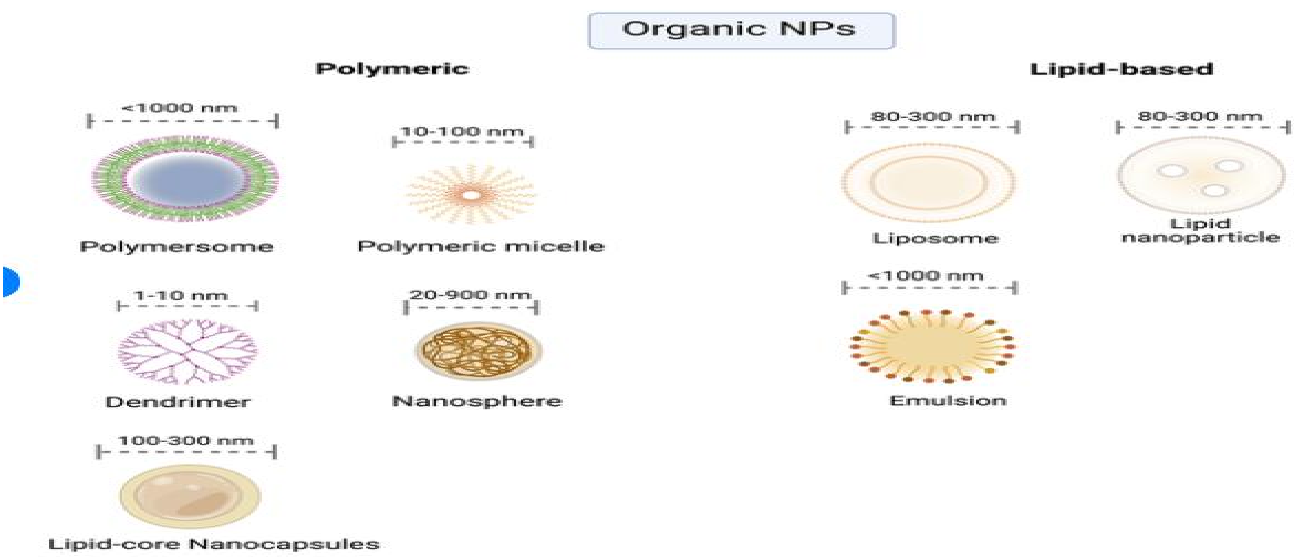


Figure 5 : Organic NPs type (Lokole et al., 2024).

I.3.2.2.3. Inorganic NPs

Inorganic NPs are NPs that lack carbon atoms and are known as inorganic nanoparticles. Inorganic NPs (figure 6) are typically classified as those composed of metal-based, metal oxide-based, ceramic and semiconductor NMs (Mekuye & Abera, 2023). Due to their unique structural and compositional characteristics, inorganic NPs exhibit distinct size-dependent physical properties, including optical, magnetic, electronic, and catalytic behaviors (Rizwan et al., 2021).

Inorganic NPs provide substantial advantages in the biomedical field due to their physical properties, high surface area, tunable structures, versatile surface chemistry, and distinctive optical (Liu et al., 2020). In the biomedical and biotechnological fields, such properties have been harnessed in the development of various inorganic NPs, including iron oxides, gold, silver, silica, and quantum dots (Rizwan et al., 2021).

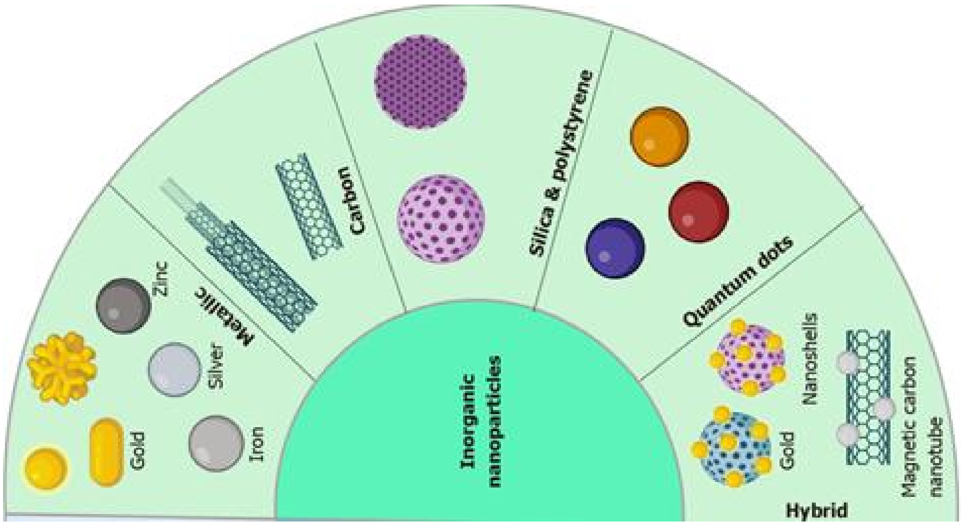


Figure 6 : Inorganic NPs types (Gogoi et al., 2022).

I.3.2.2.3.1. Metal based NPs

Metal-based NPs can be synthesized through destructive or constructive processes. Aluminum (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag), and zinc (Zn) are metal materials that are frequently used in NPs synthesis (Mekuye and Abera, 2023; de Jesus et al., 2024).

Their nanoscale size (typically between 10-100 nm) and distinctive surface characteristics such as their shape, crystal facets, and size of MNPs play a critical role in determining their physical and chemical properties, as well as their method of synthesis. Additionally, factors such as shape (spherical, rod-shaped, hexagonal, tetragonal, cylindrical, or irregular), optical properties (including colour), and environmental conditions (such as exposure to sunlight, moisture, air, and heat) further influence the properties and performance of MNPs (Sune et al., 2024).

I.3.2.2.3.2. Metal oxide-based NPs

Metal oxide NPs, also known as metal oxide NMs , are composed of positive metallic ions and negative oxygen ions. Examples of metal oxide NPs that are frequently synthesized include silicon dioxide (SiO_2), titanium oxide (TiO_2), zinc oxide (ZnO), and aluminum oxide (Al_2O_3). These nanoparticles exhibit remarkable properties compared to their metal analogs (Mekuye & Abera, 2023).

I.3.2.2.3.3. Ceramic NPs

Ceramic NMs are ultra-small particles and inorganic solids made up of carbides, carbonates, oxides, carbides, carbonates, and phosphates synthesized via heat and successive cooling to attain desired properties (Altammar, 2023; Mehta et al., 2023). These NPs can exhibit a variety of structural forms, including amorphous, polycrystalline, dense, porous, and hollow morphologies (Altammar, 2023). Ceramic NPs are widely regarded as highly effective carriers for therapeutic agents such as drugs, genes, proteins, and imaging agents (Thomas et al., 2015).

I.3.2.2.3.4. Semiconductor NPs

Semiconductor NPs exhibit properties that bridge the characteristics of both metals and non-metals (Altammar, 2023).They are classified into threegroups: concentrated magnetic semiconductor NMs, non-magnetic semiconductor NMs and diluted magnetic semiconductor NMs (Mekuye & Abera, 2023). For instance, semiconductor NPs can absorb and emit light, which enables their use in developing more efficient solar cells and brighter light-emitting diodes. Additionally, they increasingly being explored for bioimaging and cancer therapy due to their optical and functional versatility (Altammar, 2023).

I.3.2.2.4. Based on number of dimensions

NMs can be classified based on their dimensionality (Figure 7). Zero-dimensional (0-D) NMs have all three dimensions within the nanoscale and include examples such as quantum dots, and fullerenes. One-dimensional (1-D) NMs have two nanoscale dimensions and one dimension that extends beyond the nanoscale; examples are nanotubes, and nanofibers. Two-dimensional (2-D) NMs possess one nanoscale dimension while the other two dimensions are larger, such as nanodiscs, and nanolayers. Finally, three-dimensional (3-D) or bulk NMs are not confined to the nanoscale in any dimension and include embedded clusters and equiaxed crystallites (Joudeh & Linke, 2022).

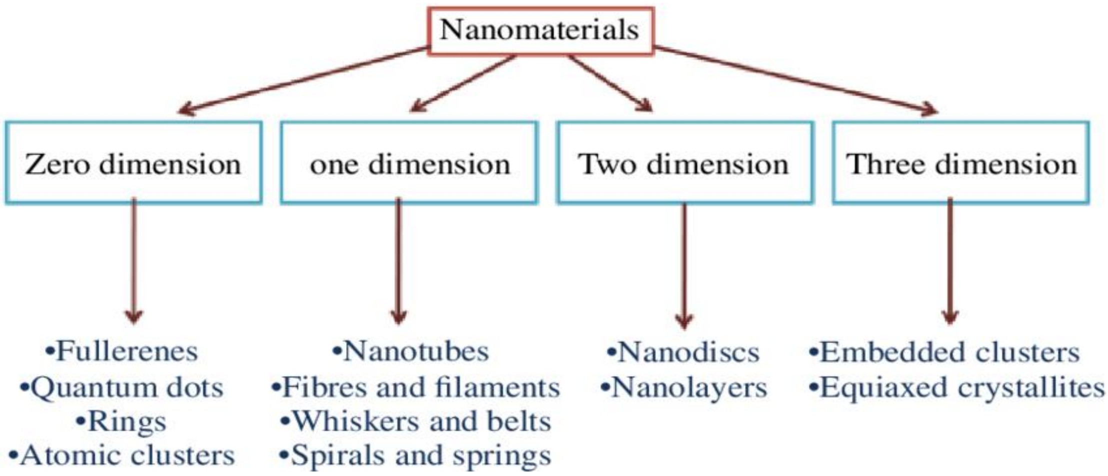


Figure 7: Classification of NMs on the basis of dimensions (Singh et al., 2020).

I. 3.2.2.5. Based on pore dimensions

NMs can be classified by pore size into mesoporous, microporous, and macroporous types (Figure 8). Mesoporous NMs (2-50 nm) have a high surface area and tunable structure. Microporous NMs (< 2 nm), like zeolites, are ideal for air filtration and gas separation. Macroporous nanomaterials (> 50 nm) offer excellent transport properties and are suitable for drug delivery due to their large pore sizes and efficient molecular diffusion (Harish et al., 2022).

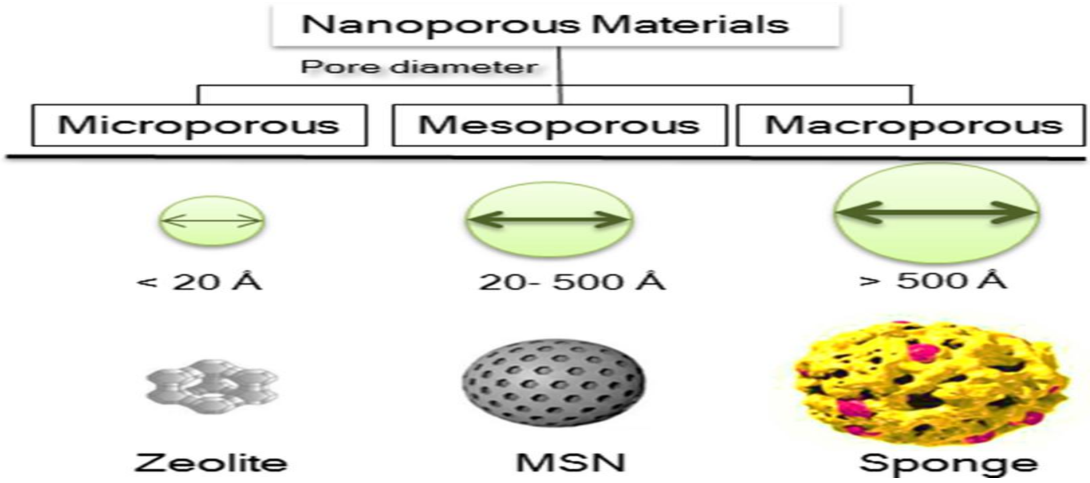


Figure 8: Classification of NMs based on pore diameter (Niazian et al., 2021).

I.3.2.2.6. Based on potential toxicity

NMs are classified by toxicity into fiber-like NPs, biopersistent granular NPs, and carcinogenic, mutagenic, asthmagenic, reproductive toxins NPs (CMAR). Fiber-like NPs include carbon nanotubes with exposure limits of 10^4-10^5 fibers/m^3. Biopersistent granular NPs , such as metal oxides and metals, have limits around 2×10^7 particles/m^3 or 0.3 mg/m^3 for insoluble forms. CMAR NPs , including nickel and cadmium-based particles, pose serious health risks, with exposure limits between 2×10^7 and 4×10^7 particles/m^3 (Mekuye & Abera, 2023).

I.4. Use and advantages of nanotechnology

The discovery of new materials, phenomena, and processes at the nanoscale, along with the advancement of innovative theoretical and experimental research techniques, offers unique opportunities for developing inventive nanostructured materials and nanosystems. There are many current and anticipated advancements in nanoscience and nanotechnology concerning their applications in medicine, healthcare, energy, environment, and the food industry. These developments are occurring at an accelerating rate (Zare et al., 2023).

I.4.1.Medcine and health care

Nanotechnology has evolved into a promising field with substantial potential for innovation across various healthcare and biomedical applications (Raffa et al., 2010). These applications (Figure 9) involve a number of medical fields such as drug delivery, tissue engineering, gene delivery, medical diagnostics and cancer therapy (Xiaohan et al., 2024).

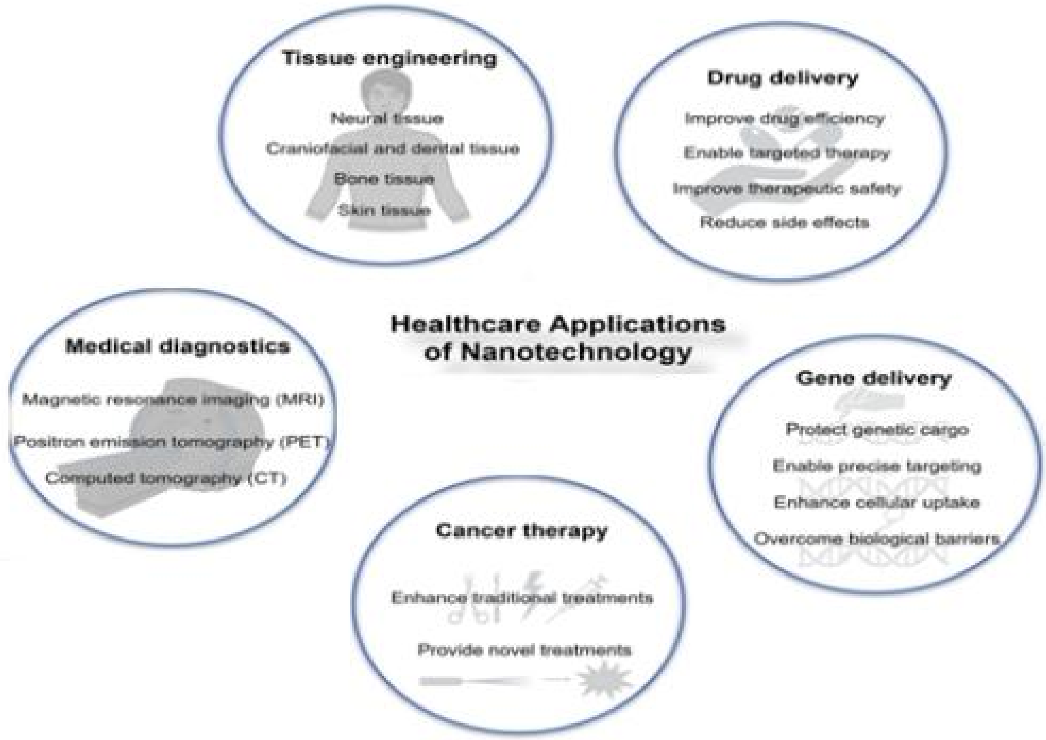


Figure 9: Applications of nanotechnology in healthcare (Xiaohan et al., 2024).

I.4.1.1.Drug delivery

The most impactful uses of nanotechnology is in targeted drug delivery (Valentina et al., 2011). NPs can be designed to encapsulate therapeutic agents, thereby enhancing their solubility and stability. This targeted approach enables higher drug accumulation at disease sites while reducing systemic side effects (Kazi et al., 2024).

I.4.1.2. Regenerative medicine and tissue engineering

Regenerative medicine is an interdisciplinary field of medical applications that combines the advantages of cell therapy and tissue engineering to develop mechanisms for the treatment, monitoring, maintenance, regulation, construction, improvement, protection, and repair of damaged or dead cells, tissues, and organs (Boisseau & Loubaton, 2011; Malik et al., 2023).

NPs are increasingly used in medical applications such as tissue engineering. Various NPs such as silver, gold, quantum dots, metal oxides, and carbon nanotubes exhibit useful traits and make them valuable in enhancing the biological and mechanical performance of tissue engineering scaffolds. NPs are advantageous due to their small size, large surface area-to-volume ratio, and similarity to natural cellular and extracellular components (Sardari et al., 2024).

➢ **Bone tissue engineering**

Tissue repair has advanced significantly with the powerful regenerative capabilities of nanoassemblies (Patrick et al., 2011). Using nanotechnology, it is possible to regenerate or restore damaged borne tissue (Figure 10). Three key factors are required for successful bone regeneration (Bauso et al., 2024):

- Stem cells which are able to form a functional;
- Specific growth factors that stimulate cell migration, proliferation, differentiation, and vascularization;
- Biomaterials that offer a three-dimensional (3D) matrix for cell adhesion and growth.

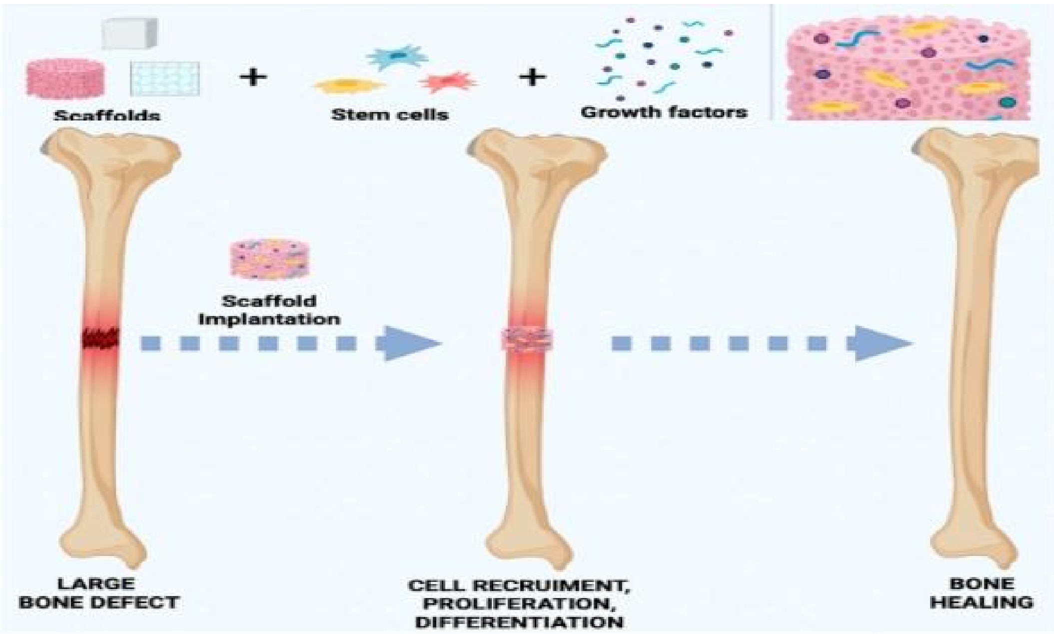


Figure 10: Bone regeneration approach (Bauso et al., 2024).

- **Skin tissue engineering**

Tissue engineering focuses on using cells and scaffolds to grow new tissues and organs such as skin tissue. Cells can proliferate and differentiate within 3D scaffolds, which are enhanced by growth factors (Figure 11) to guide cellular behavior toward tissue regeneration (Sardari et al., 2024).

Figure 11: Skin engineering tissue approach (Habibzadeh et al., 2022).

I.4.1.3. Gene delivery

The development of safe and efficient gene delivery systems is crucial for effectively transporting gene-based drugs to targeted tissues, cells, and organelles (Jiang et al., 2023). Recently, NPs have become popular as nanocarriers for gene delivery in an attempt to enhance the cellular uptake, effectiveness, as well as targeted delivery and limited toxicity. Nanocarriers can protect recombinant DNA and RNA molecules from enzymatic degradation and achieve a higher transmembrane efficiency compared to other carriers (Shen et al., 2019). The(Figure 12) indicated the multi-step process involved in gene delivery, including (1) DNA condensation, (2) cellular uptake, (3)endosomal escape, (4) intracellular trafficking, (5)nuclear translocation, and (6) transcription**.**

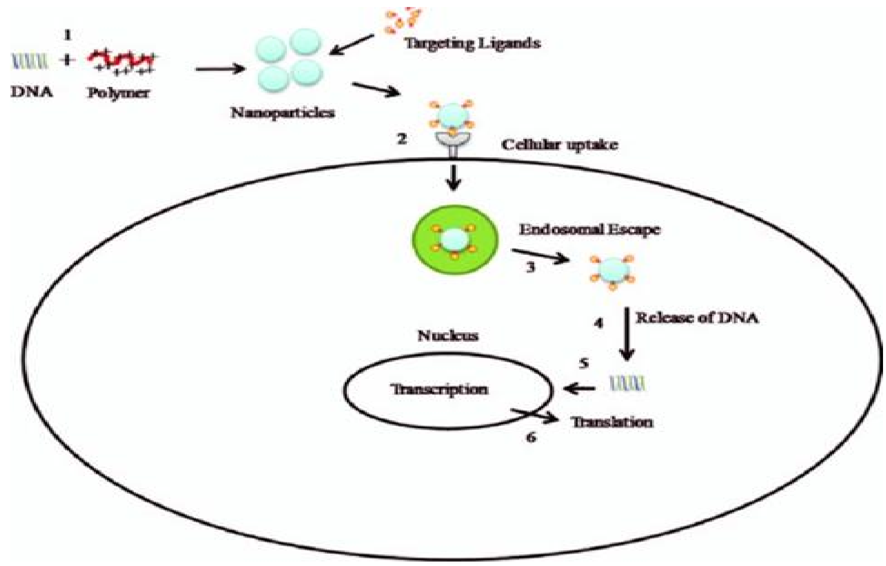


Figure 12: Multi-step process involved in gene delivery (Arya, 2014)

I.4.1.4. Medical diagnostics

Nanotechnology accelerates diagnostic processes with many nano-devices and nano-biosensors, which have been innovated to monitor the bio- molecules, at a very low concentration resulting in rapid detection of disease and genetic disorders at an early stage (Patel et al., 2015; Abid et al., 2023). Nanotechnology applied to cancer detection employs NPs-ligand complexes that attach to specific genetic mutations, When these complexes are paired with contrast agents, they can highlight tumor cells. This method holds promise for enabling the early identification of metastatic potential (Farzad et al., 2023).

In situ diagnostic devices, like capsule endoscopy cameras, have demonstrated clinical success. These devices are capable of detecting and imaging internal bleeding sites and other issues through oral ingestion, so tiny that a patient can directly swallow it (Lee et al., 2021). Capsule endoscopy cameras (Figure 13) is a particular endoscope with imaging equipment, batteries, light source, and a signal-transmitting component. It can move passively within a patient’s gastrointestinal environment and examine the patient’s lesions under external control such as magnetic control. Then, this capsule endoscopy cameras will output a large amount of video information for the physicians’ examination to determine the disease and follow-up treatment plan (Bai et al., 2022).

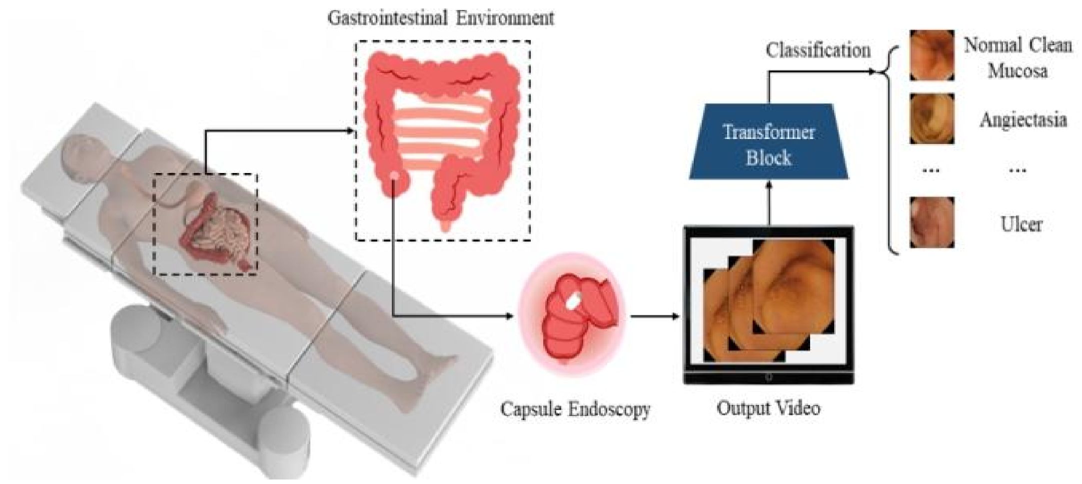


Figure 13 : Capsule endoscopy system (Bai et al., 2022).

I.4.1.5. Cancer therapy

Targeted delivery of anti-cancer drugs remains a major obstacle due to poor drug availability at tumor sites, drug resistance, and harmful side effects associated with conventional therapies. Nanotechnology offers significant potential to improve cancer diagnosis and treatment by enabling the design of materials specifically engineered to target cancer cells (Biswas et al., 2014).

Various nanotechnology based drug delivery systems that have been employed for cancer detection and treatment (Misra et al., 2010) includes NPs, liposomes, nanocantilever, carbon nanotubes, and quantum dots (Figure 14).

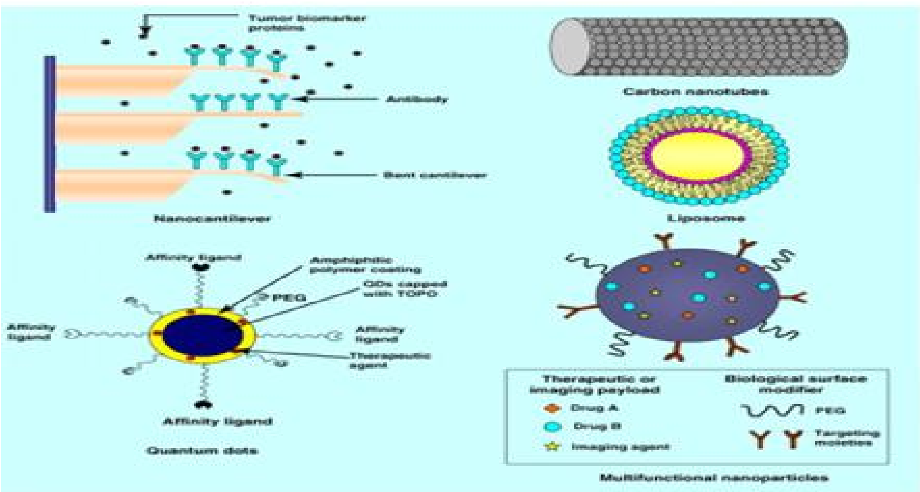


Figure 14: Different nanotechnology- based tools used in cancer therapy (Misra et al., 2010).

I.4.2. Energy sector

Nanotechnology holds the potential to transform the energy sector by improving sustainability, boosting efficiency, reducing costs across the entire energy value chainfrom production, conversion, storage and utilization (Figure 15). Additionally, its applications aim to include a more reliable and eco-friendly energy supply and minimized environmental impact (Milosavljević & Pantić, 2019).

The application of nanotechnology enhances the efficiency of production (Mojtaba et al., 2020; Zafar et al., 2023). Nanotechnology is integral to advancing energy storage technologies, particularly in batteries, supercapacitors, and fuel cells (Aithal., 2016). Innovations at the nanoscale can lead to more efficient and smaller batteries, fuel cells, and solar cells (Jin, 2021).

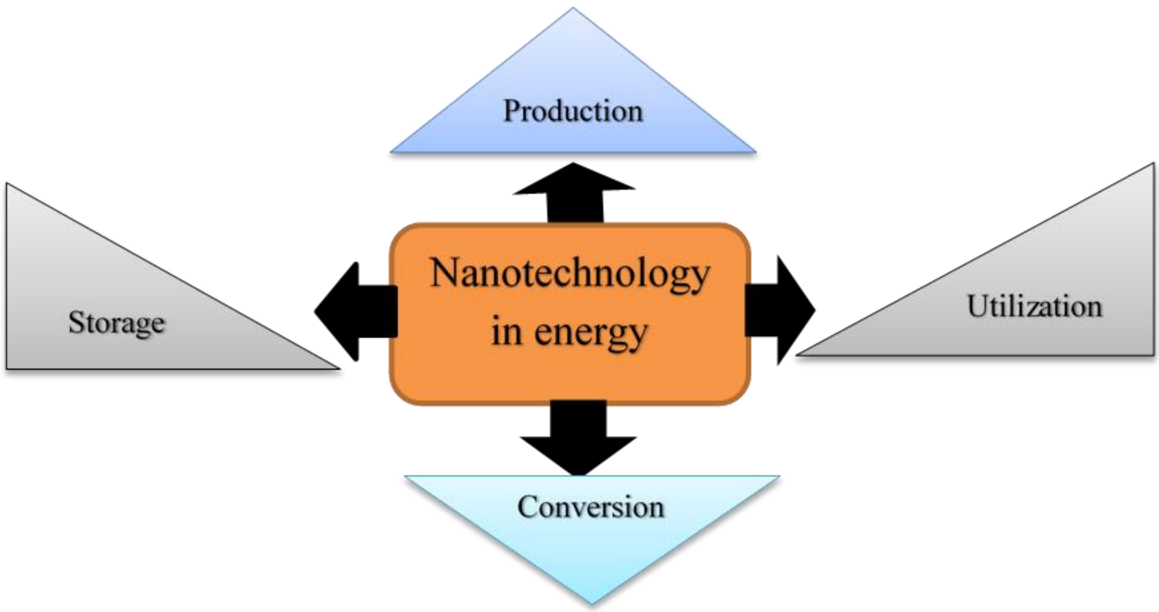


Figure 15: Nanotechnology use in energy sector (Personal picture).

High-efficiency NMs significantly improve hydrogen storage, contributing to the development of more energy-efficient vehicles. Additionally, these materials enhance battery performance by increasing power output, reducing charging time, improving safety (Aithal, 2016). Nanotechnology provides a range of solutions for conserving energy, such as lightweight nanocomposites in vehicles, improved engine components and fuel additives (Timmer, 2008).

I.4.3. Environnement

NPs are playing a growing role in environmental cleanup thanks to their cost-effectiveness, high efficiency, and the small quantities needed for treatment (Yousaf et al., 2022). Various nanotechnologies, such as nano zero-valent iron, silver NPs, carbon nanotubes, and others, are widely used in environmental applications (Figure 16) including water treatment, (Kumar et al ., 2017) . Additionally, nanotechnology finds use in waste management approaches (Pournaras et al., 2018).

They contribute to the treatment of sewage and sludge, and support water purification particularly in the food and dairy industries through nanofiltration. In addressing soil contamination, NPs are introduced into targeted areas to break down or neutralize pollutants such as heavy metals (Yousaf et al., 2022). For example, nano zero-valent iron removes contaminants through chemical reduction, involving physical destruction of organic pollutants and immobilization of heavy metals and radionuclides (Xu et al., 2017).

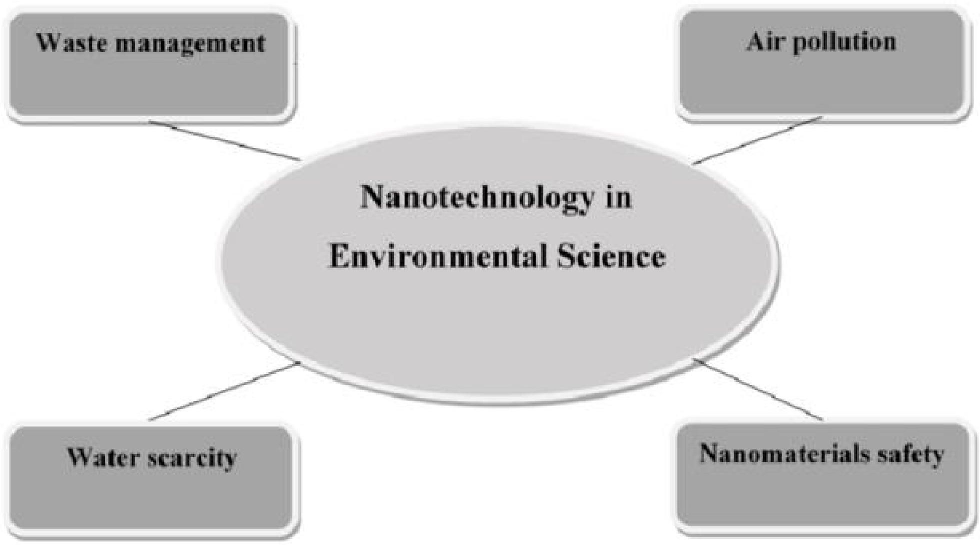


Figure 16: Important usage of nanotechnology in environmental science (Mojtaba et al., 2020).

I.4.4. Food industry

Nanotechnology is advancing packaging solutions by developing materials that boost product safety (Bhuyan, 2017). Microbial contamination in weaning foods can cause infections and poor nutrition, making bacterial control crucial in food production and storage. Nanoantimicrobials offer a promising solution by preventing spoilage and extending food shelf life (Wang & Lim, 2016).

NPs in food processing improve quality, health benefits flavor and stability. It can also be used to modify food taste and color (Mensah et al., 2023). Approved NMs like SiO_2 (E551) and TiO_2 (E171) are used as additives (Mahmoud, 2015).(The Figure 17) indicated role of nanotechnology in different aspects of food sectors.

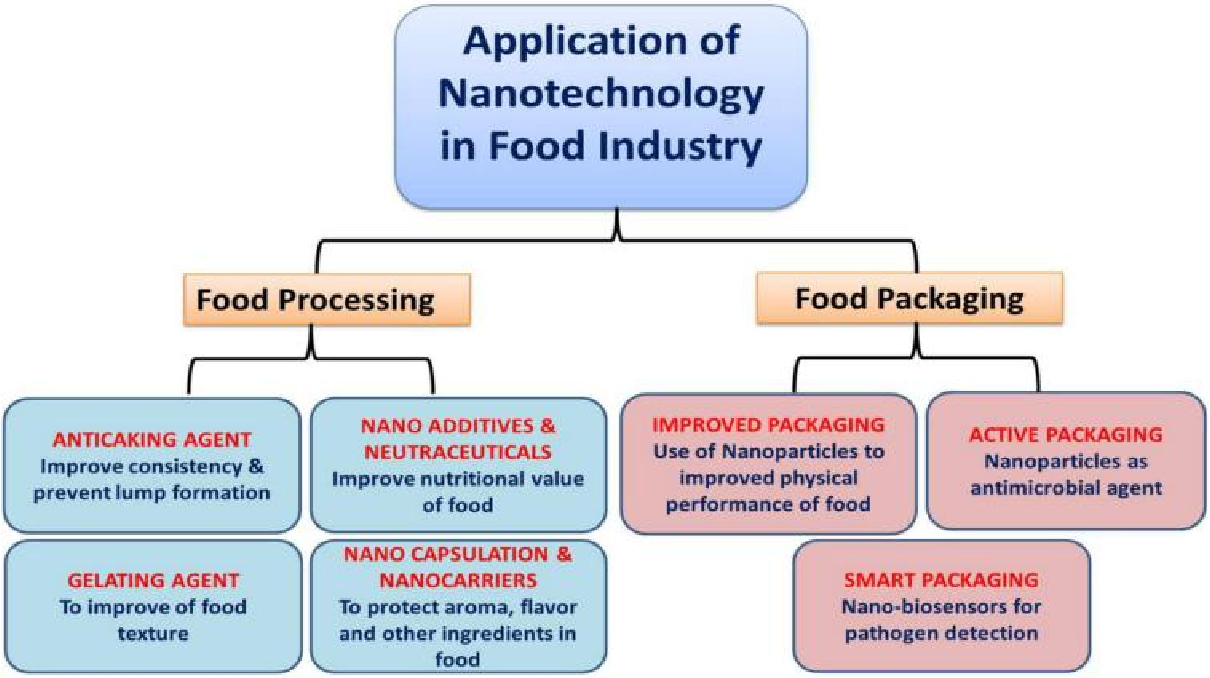


Figure 17: Schematic diagram showing role of nanotechnology in different aspects of food sectors (Sharma et al., 2017).

I.6. Nanomaterials toxicity

I.6.1. Toxicity in organs and cells body

There are nanomedicine that involve subcutaneous or intravenous injectable nanoparticulate systems. These carry and deliver the drug directly into human body, these NPs carriers may be responsible for the toxicity as they would interact with the biological macromolecules and result in toxicity. Alternately, insoluble NPs can accumulate inside tissues or organs and lead to toxicity (Limaye et al., 2014).

The lung and liver are the main target tissues after exposure to silver NPs via inhalation for 90 days, and the resulting toxicity is dose-dependence (Zhang et al., 2022). Exposure to carbon NMs can cause lung inflammation, granuloma, and fibrosis. Carbon, Ag, and Au nanomaterials can reach also other organs such as central nervous system. Quantum dots, carbon, and TiO_2 NPs can go through the skin barrier. MnO_2, TiO_2, and carbon Nps may enter the brain via olfactory neurons in the nasal epithelium (Barhoum et al., 2022). (Figure 18) indicated the NPS exposure routes in the human body, the organs/tissues concerned, and the diseases linked to such exposure.

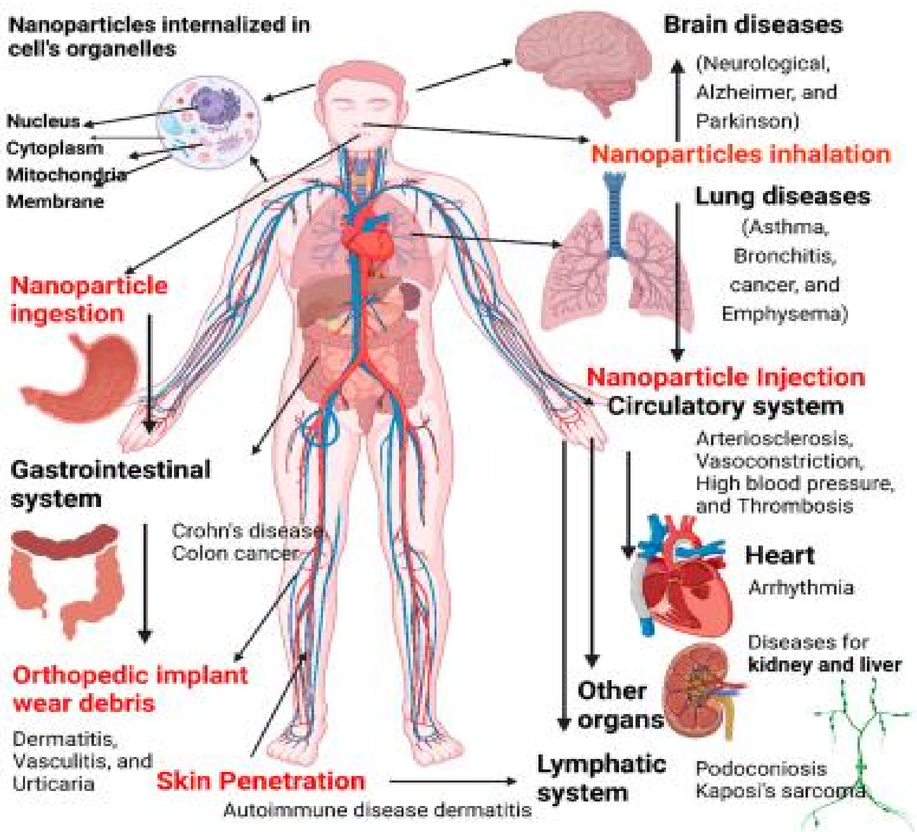


Figure 18: Schematic representation of the NPs exposure routes in the human body, the organs/tissues concerned, and the diseases linked to such exposure (Harish et al., 2022).

Mechanisms on the nano-bio interface can be either chemical or physical. Chemical mechanisms include the production of reactive oxygen species (ROS). ROS is considered as being the main underlying chemical process in nanotoxicology, leading to secondary processes that can ultimately cause cell damage and even cell death such as mitochondrial and DNA damage. Moreover, ROS is one of the main factors involved in inflammatory processes. Physical mechanisms at the nano-bio interface include disruption of membranes (Elsaesser & Howard, 2012). For example, silver NPs can interact with with Na and K ion channels on the cell membrane, causing an imbalance in the cell membrane potential (Zhang et al., 2022).

Lastly, membrane stability can be affected by NPs either indirectly (oxidation) or directly (physical damage) which can lead to cell death. Research has shown that different NMs can damage membranes by various processes (Figure 19) leading to a compromise of membrane integrity and stability as well as the formation of nanosized holes (Elsaesser & Howard, 2012).

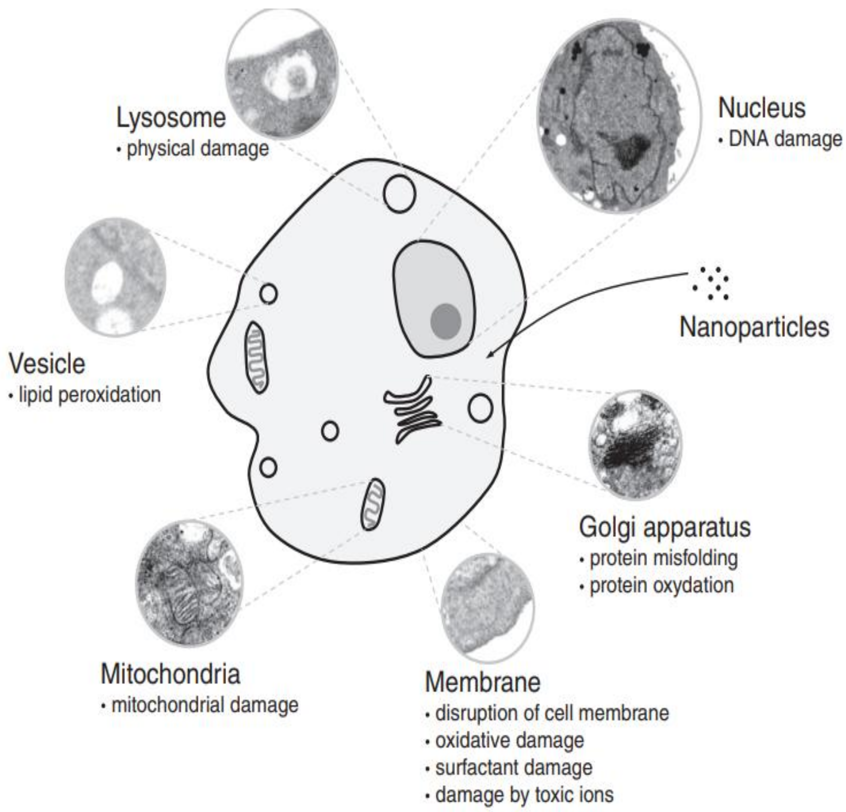


Figure 19: NPs interaction with cells (Elsaesser & Howard, 2012).

I.6.2. Toxicity in environment

NPs exploited for environmental engineering applications and may also display toxicity towards the environment and the organisms present in the ecosystem (Barhoum et al., 2022). NPs released into the environment interact with air, water and soil can change the surface properties of the particles, which can result in particle aggregation or changes in particle charge, and other surface properties (Elsaesser & Howard, 2012). The Table III mentioned nanoparticles certain environmental risk of NPs use.

Table III: Environmental risks of NMs (Barhoum et al., 2022).

Environmental type	Environmental risks
Air	NPs can be formed in industrialized areas are directly emitting carbonous NPs to the atmosphere. They classify as nanosized pollutants.
Soil	MNPs from the utilized biomass can be transferred to soil. Therefore, the high Ag concentration in the resulting biomass would act as an inhibitor of bacterial growth including the beneficial microorganisms present in the soil, such as nitrogen-fixing bacteria.
Water	Antimicrobial metal and metal oxide NPs have a toxic effect in nematodes suggesting that cumulative exposure to silver NPs might significantly affect the ecological balance of aquatic environments.
Microorganisms	Toxicities associated with NPs in microorganisms causes membrane disorganization, generation of ROS, and in some cases, oxidative DNA damage.
Plants	The Zn and Al containing NPs negatively affect germination and root growth of agriculturally relevant plant species.

Chapter II

herbal medicine

II. Herbal medicine

II.1. Definition

Pharmocognosy studies medicines originating from natural sources (Figure 20), encompassing plants, animals, and microorganisms. The field's scope relies on knowledge regarding the safety, purity, and efficacy of complex multicompound products (Leisegang, 2021). Most pharmocognosy research has focused also on identifying controversial plant species and authenticating commonly used traditional medicinal plants through morphological, phytochemical, and physicochemical analysis (Chanda, 2014).

Utilizing medicinal plants for both preventing and treating illnesses is what defines herbal medicine (Firenzuoli & Gori, 2007). They may provide therapeutic benefits, especially when used as complementary medicine (Oladimeji, 2024). This practice encompasses a wide spectrum, from age-old folk remedies found in every nation to the application of carefully measured and refined plant extracts (Firenzuoli & Gori, 2007).

Figure 20: Herbal medicine utilizing medicinal plants (Tehran, 2025).

II.2. History

According to ancient Babylonian accounts, the use of plants as medicine goes back 60,000 years. Written records on herbal medicine in Egypt and China date back approximately 5000 years, and in Asia Minor and Greece, they date back 2500 years. Various herbal medicinal systems exist, and the practices and philosophy of each are shaped by the region where it first developed. In China, they have their own system known as Traditional Chinese (Msomi & Simelane, 2018).

The Chinese book on roots and grasses "Pen T Sao," authored by Emperor Shen Nung around 2500 BC, describes 365 drugs (dried parts of medicinal plants). Many of these, such as camphor, ginseng, jimson weed, cinnamon bark, and ephedra, are still in use today (Petrovska, 2012).

II.3. Classification of herbs

II.3.1. According to the usage

Herbs can be categorized into four main types: medicinal, culinary, aromatic, and ornamental. Medicinal herbs are important in everyday life for medicine, cooking, and cosmetics. But the large number of plant species makes classification difficult (Amgad & Suliman, 2020). Culinary herbs and spices enhance food's flavor, aroma, and appearance. Herb and spice blends typically contain only those ingredients, while seasoning mixes may also include additives like thickeners, preservatives, and colourings to improve taste, nutrition, or functionality (Joanna & Maria, 2024).

The use of purified essential oils in food, cosmetics, and fragrances has increased significantly. About 90% of essential oil production is used in food flavouring and perfumes. Classifying these oils by quality and purity is essential for making high-quality products. Essential oils are complex, low-concentration mixtures from plants, typically extracted through methods like hydro-distillation, centrifugation, steam distillation, and cold pressing (Mansour et al., 2021).

II.3.2. According to the active constituents

Herbs are classified into five main categories based on their active compounds: Aromatic (volatile oils), Astringent (tannins), Bitter (phenol compounds, saponins, and alkaloids), Mucilaginous (polysaccharides), and Nutritive (food substances). Bitter herbs, traditionally used to support digestion, may work by triggering a cephalic response that increases peripheral vascular resistance. This response helps maintain blood pressure during digestion by supporting the cardiovascular system's ability to handle increased blood flow to the digestive organs (Michael et al., 2015).

Mucilage is a gelatinous substance that occurs in many plants composed of proteins and polysaccharides. It exists in different plant parts such as leaves, seed coats, roots, bark, and the middle lamella. (Poonam & Bhavya, 2022). Nutritive herbs such as wheat germ and related herbs are recognized for their rich nutritional content. They are considered true foods, providing both health benefits such as fiber, mucilage, and diuretic properties and essential nutrients like proteins, carbohydrates, fats, vitamins, and minerals. Examples spirulina (Yudharaj et al., 2016).

II.3.3.According to their taxonomy

This classification is based on plant taxonomy, which relies on morphological characteristics. In contrast to animals and some microorganisms that typically excrete their final metabolites, plants tend to store these compounds within their tissues. While many plant metabolites were once believed to be specific to certain species, it is now understood that compounds like alkaloids and isoprenoids are broadly distributed throughout the plant kingdom (Yudharaj et al., 2016).

II.3.4. According to the period of life

Herbs can be classified into annuals, biennials, and perennials. Annual herbs complete their life cycle in one year, including basil, chamomile, cilantro, and saffron. Perennial herbs live for multiple seasons, such as mint, sage, thyme, rosemary, and lavender. Most can be started from young plants, except parsley. Biennial herbs live for two years and bloom in the second season, including caraway, primrose, and mullein (Bishnoi, 2016).

II.3.5. According to the nature

Medicinal plants have long been used by humans across cultures for their healing properties. Through observation and experience, early humans identified their therapeutic effects, leading to a growing body of knowledge that supports their use in both traditional and modern medicine. These plants remain vital to global health due to their diverse active compounds and wide-ranging medicinal potential (Awotedu et al., 2020).

II.4. Phytochemicals of medicinal plants

Phytochemicals are natural, biologically active compounds in plants that benefit human health and protect plants from environmental stress, disease, and damage. They also influence the cellular functions, plant's color, scent, and flavor (Mamta et al., 2013; Elda et al., 2024). The relatively recent advances in biochemistry have greatly clarified the interplay between enzymatically catalysed reactions of the primary metabolites. These metabolites lead to secondary metabolites (Figure 21), so called because it is obvious his role in the metabolism of many organisms (Ilori et al., 2023).

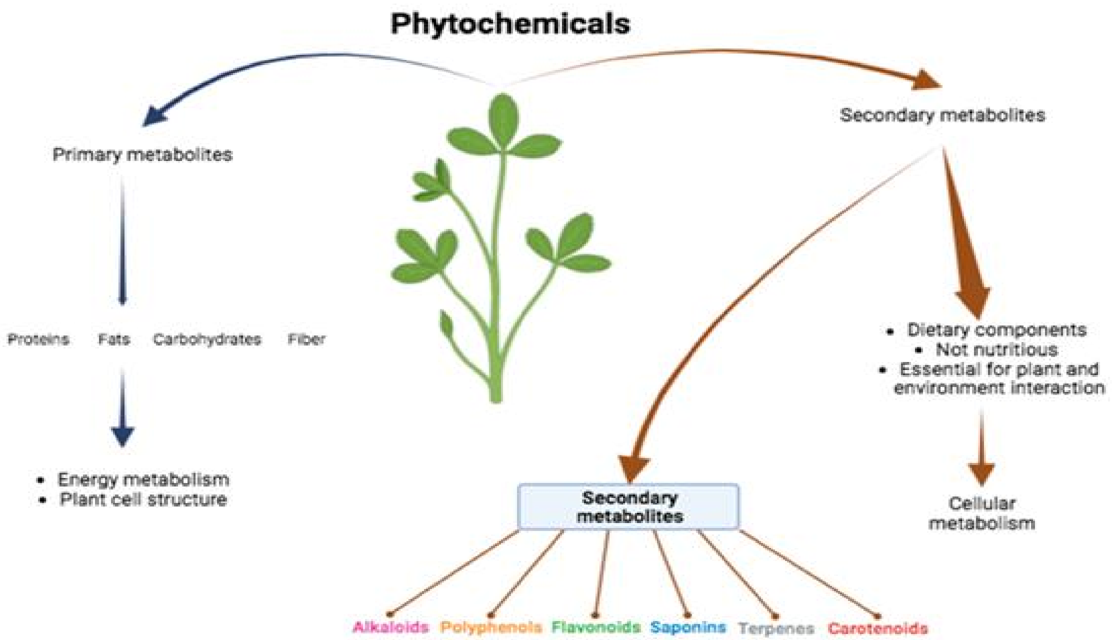


Figure 21: The primary and secondary metabolites (Elda et al., 2024).

II.4.1.Primary metabolites

Primary metabolites are essential for plant survival and development, encompassing compounds such as carbohydrates, amino acids, proteins, lipids, and the purine and pyrimidine bases found in nucleic acids (Fatemeh et al., 2022). Primary metabolites are essential for growth and development, often acting as biocatalysts. Universally present in living organisms, they support key processes like photosynthesis, respiration, and nutrient assimilation. They are also used as industrial raw materials and food additives (Geetha, 2014).

II.4.2. Secondary metabolites

Secondary metabolites, especially phytochemicals, have therapeutic value and play a key role in disease treatment. These include alkaloids, terpenoids, phenols and flavonoids, and saponins, tannins and steroids (Sayantan & Ramachandra, 2019).

II.4.2.1. Phenolic acids

The term "phenolic acids" refers to phenolic compounds that feature a single carboxylic acid functional group (Figure 22). Naturally occurring phenolic acids are primarily based on two structural types: hydroxybenzoic and hydroxycinnamic acids. They help protect against oxidative stress-related diseases by neutralizing free radicals, supporting other antioxidants, and activating protective enzymes (Onyenibe et al., 2023).

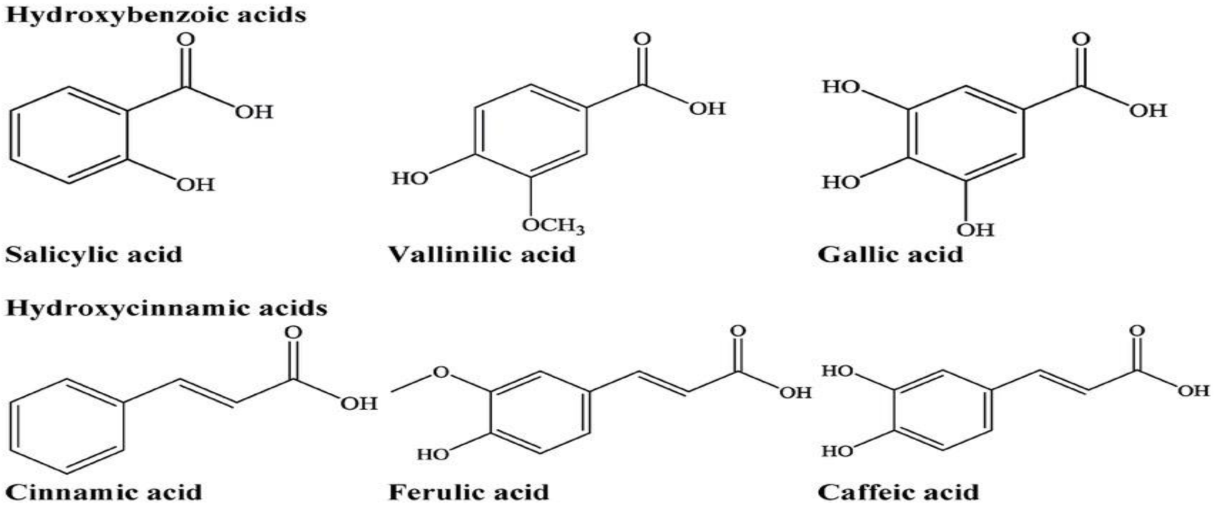


Figure 22: Structures of the important naturally occurring phenolic acids (Mamta et al., 2013).

II.4.2.2. Flavonoids

Flavonoids are a group of compounds characterized by a fifteen-carbon skeleton, comprising two aromatic benzene rings (A and B, as illustrated in (Figure 23) connected by a heterocyclic pyran ring (C). They are categorized into various classes, including flavones (such as flavone, apigenin, and luteolin), flavonols (such as quercetin, kaempferol, myricetin, and fisetin), and flavanones (such as flavanone, hesperetin, and naringenin), among others (Kumar & Pandey, 2013).

Flavonoids are bioactive compounds with anti-inflammatory, antiviral, anticarcinogenic, and enzyme-inhibiting properties (Roy & Bharadvaja, 2022). Flavonoids rich plants can also preventing cardio metabolic disorders and supporting cognitive function with aging (Ullah et al., 2020). In plants, they enhance color and aroma to attract pollinators, support reproduction, and protect against environmental stress, while also aiding in drought and cold tolerance (Roy & Bharadvaja, 2022).

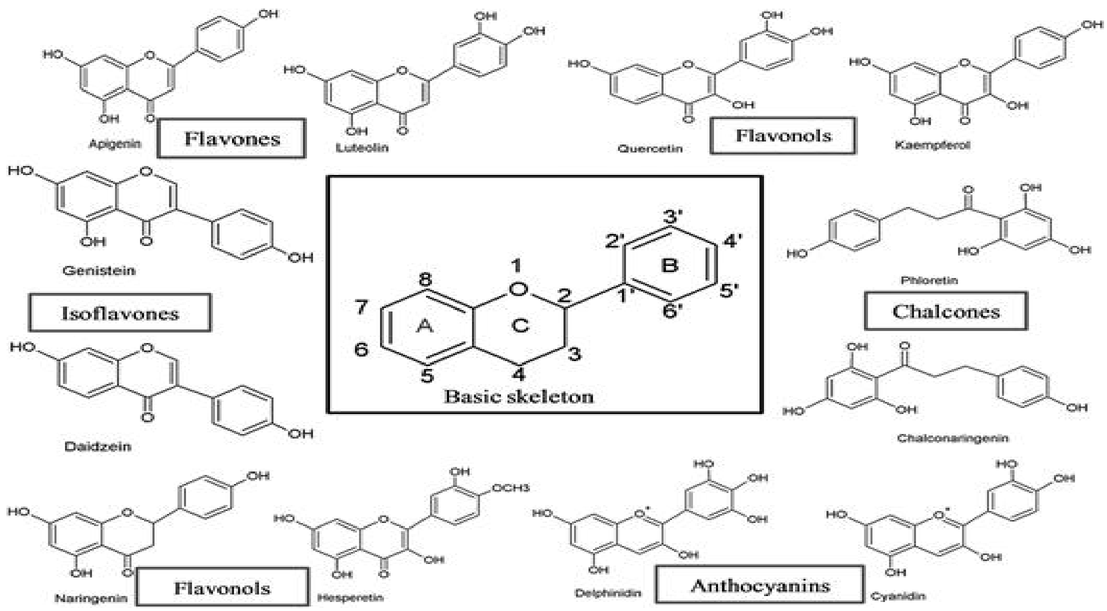


Figure 23: Structure of basic skeleton of flavonoid and various classes (Panche et al., 2016).

II.4.2.3.Tannins

Tannins are polyphenolic compounds, classified into hydrolysable such as gallotannin and non-hydrolysable or condensed types such as phlobatannin (Figure 24). They found in many edible plants like tea, berries, and grapes (Kamarudin et al., 2021). Tannin consumption has been linked to multiple health benefits and may help reduce the risk of chronic diseases such as aiding blood clotting, lowering blood pressure, and acting as antioxidants (Mamta, 2013; Kamarudin et al., 2021). They serve as a natural defense in plants (Kamarudin et al., 2021).

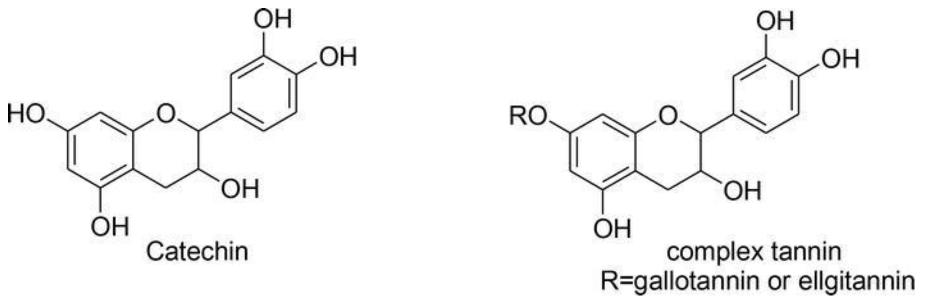


Figure 24: General structure of complex tannins (Al Mamari & Al-Abri, 2021).

II.4.2.4. Alkaloids

They are among the major and most abundant compounds produced by plants, formed as metabolic by products derived from amino acids (Misganaw, 2022). It was found that they were nitrogen-containing bases, which formed salts with acid (Figure 25). These alkaloids are used as the local anesthetic .and stimulant as cocaine. Almost all the alkaloids have a bitter taste. The alkaloid quinine for example is one of the bitterest tasting substances known (Mamta, 2013).

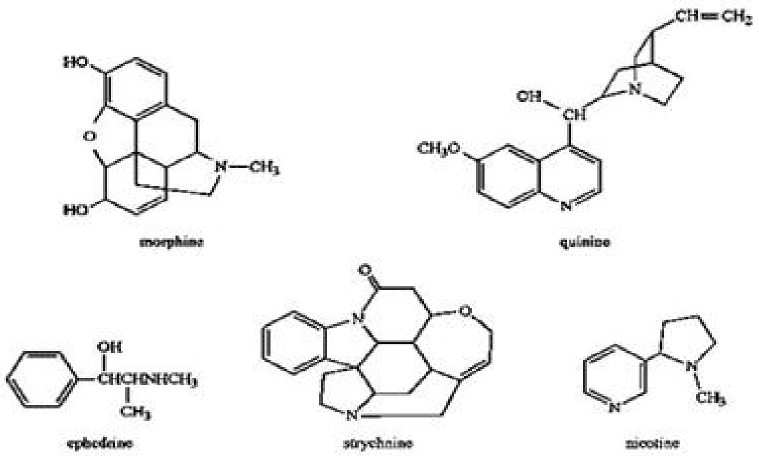


Figure 25: Structures of some alkaloid (Nadia & Eleazar, 2018).

II.4.2.5. Steroids

Steroids are a class of natural or synthetic organic compounds defined by a core structure of 17 carbon atoms arranged in four interconnected rings (Figure 26). Synthetic steroids with therapeutic applications include numerous anti-inflammatory drugs, anabolic agents that promote growth, and oral contraceptives (Clayton et al., 2025). Plant steroids exhibit diverse medicinal, pharmaceutical, and agrochemical activities, including anti-tumor, immunosuppressive, hepatoprotective, antibacterial, cytotoxic, and cardiotonic effects (Snehal et al., 2015).

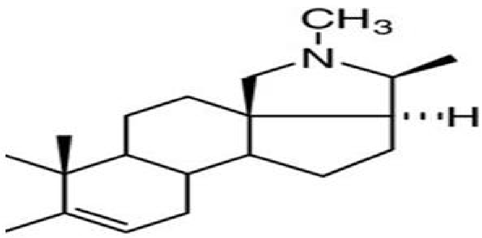


Figure 26: Structure of steroids (Kasal, 2010).

II.4.2.6. Saponins

Saponins are bioorganic compounds with a glycosidic bond at C-3, connecting an aglycone to a sugar chain. They are high-molecular-weight amorphous solids, with the aglycone part containing 27–30 carbon atoms (Maher et al., 2019). Chemically, saponins are classified as glycosylated steroids, triterpenoids, or steroid alkaloids (Sayantan & Ramachandra, 2019). Hydrolysis splits them into aglycone and sugar moieties. Saponins have demonstrated a range of biological activities, including hypoglycemic, virucidal, antifungal, antimicrobial, and hypolipidemic effects (Kumar et al., 2023). (Figure 27) show their chemical structure.

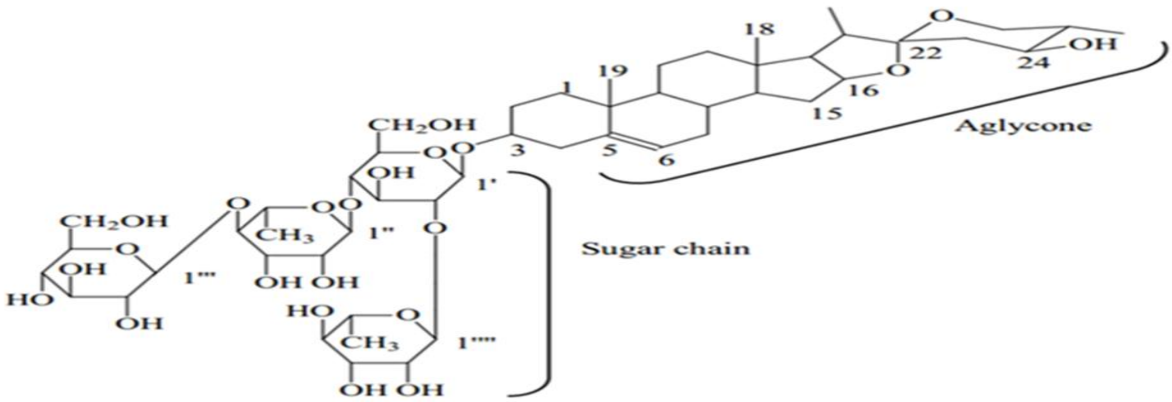


Figure 27: Chemical Structure of saponins (Nguyen et al., 2015).

II.5. Characteristics

II.5.1. Traditional and medicinal use

Medicinal plants, which contain active compounds to treat disease or relieve pain, play a crucial role in global healthcare, especially in developing countries where 80% of the population relies on traditional medicine. The practice of using medicinal plants for healing dates back thousands of years. Ancient civilizations identified the therapeutic properties of various plant species and used some of them for medicinal purposes (Tejal et al., 2023).

Herbs have been valued for their flavouring and aromatic properties for centuries (Bishnoi, 2016). Many plant extracts possess a variety of activities, including antimicrobial, antioxidant, and anticancer properties (Taussif et al., 2013). Herbal medicine is also commonly used to manage a wide range of conditions, including asthma, eczema, premenstrual syndrome, rheumatoid arthritis, migraines, menopausal symptoms, chronic fatigue, irritable bowel syndrome, and even cancer, among others (Abdel-Aziz et al., 2016). The Table IV indicated the medicinal properties of some medicinal plants.

Table IV Some natural plants with medicinal properties.

Plant	Family	Part used	Medicinal used	References
Alstonia boonei	Apocynaceae	Leaves, bark, roots	Used in the breast cancer and intestinal worms	(Muhammad et al., 2021)
Gloriosa superba	Liliaceae	Leaves and tubers	Antipyretic effect	
Harunganamada gascariensis	Hypericaceae	Bark, roots, and stems	Treatment of piles	
Bridelia ferruginea	Euphorbiaceae	Leaves and stem	Mouth wash	
Grandiflorum	Combretaceae	Leaves	Treatment of jaundice	
Adansonia combretum	Bombacaceae	Fruit, bark, pulp, and leaves	Treatment of fever, bladder and kidney problems, antimicrobial activity	
Acanthus Montanus	Acanthaceae	Twig and stems	Treatment of vaginal discharge, acts as antiemetic and effective for cough	
Afzelia africana	Fabaceae	Seeds, bark, leaves, and roots	Treatment of hernia and Gonorrhea	
Zingiber officinal	Zingiberaceae	Branched rhizome	anti-inflammatory and antioxidant	(Cartern, 2025).
Aloe Vera	Liliaceae	Sticky substance	many skin moisturizers	(Saleem & Imran, 2025)
Lavandula angustifolia	Lamiaceae	Leaves	Anxiety, eczema and dry skin	(Johnson, 2025)

II.5.1.1. Antioxidant activity

Medicinal plants possess antioxidant properties that help neutralize harmful free radicals linked to diseases like diabetes, cancer, and cardiovascular disorders. This protective effect is mainly due to compounds such as phenols and flavonoids, which scavenge free radicals and prevent cellular damage (Onyenibe et al., 2023).

II.5.1.2. Antibacterial activity

Extracts from medicinal plants have demonstrated antimicrobial. These plant-based compounds may act through mechanisms different from conventional drugs, making them valuable in treating drug-resistant microbes. Some compounds enhance the effectiveness of antibiotics, even if they aren't strongly antibacterial alone. (Natalia et al., 2021).

II.5.1.3. Anticancer activity

Globally, medicinal plants remain a major focus of research and screening efforts aimed at discovering more effective cancer therapies because they offer a rich source of potential anticancer agents. As with other areas of phytomedicine, their antitumor effects can arise through various mechanisms, such as targeting cytoskeletal proteins involved in cell division, inhibiting DNA topoisomerases, exhibiting antiprotease or antioxidant activities, and enhancing immune system function (Svita & Huma, 2010). A wide range of plants and plant-derived compounds have been evaluated for their anticancer potential, with several demonstrating significant effectiveness against various cancer types (Khan et al., 2019).

II.5.2. Safety and preventive use

The World Health Organization highlights medicinal plants as a valuable source for future medicines and stresses the importance of studying their safety (Siva, 2018). One of the key advantages of herbal medicine is its minimal side effects compared to synthetic drugs (Susan, 2019; Awotedu et al., 2020; Shankar, 2020). However, some risks may still be associated with its use (Susan, 2019).

Plant components have been shown to possess the ability to prevent the onset of certain diseases and support well-being (Fokunang et al., 2011; Shankar, 2020). Due to rising drug costs and growing resistance to conventional treatments, interest in traditional remedies has increased, leading to a renewed search for new chemical entities from traditional sources (Fokunang et al., 2011).

II.5.3. Synergistic use

Synergistic interactions are of vital importance in phytomedicines, to explain difficulties in always isolating a single active ingredient, and explain the efficacy of apparently low doses of active constituents in a herbal product.(Williamson, 2001), Their effectiveness is often supported by traditional use and known synergistic effects (Fabio, 2013).

II.6. Limitations in herbal medicine

Herbal medicines are increasingly popular throughout the world. Compared to modern conventional medicines, they are considered safe and are more economical (Dewi et al., 2022). However, the major challenge for the delivery of several herbal drug preparations is poor solubility, poor oral bioavailability and poor stability, which resulting in decreased biological activity (Ahmed et al., 2020). Many studies have combined herbal medicine with nanotechnology because nano-sized systems or nanoformulations can overcoming the dilemmas associated with herbal medicine (Dewi et al., 2022). The (Figure 28) indicated the deficiencies of the phytochemicals that limit their clinical application.

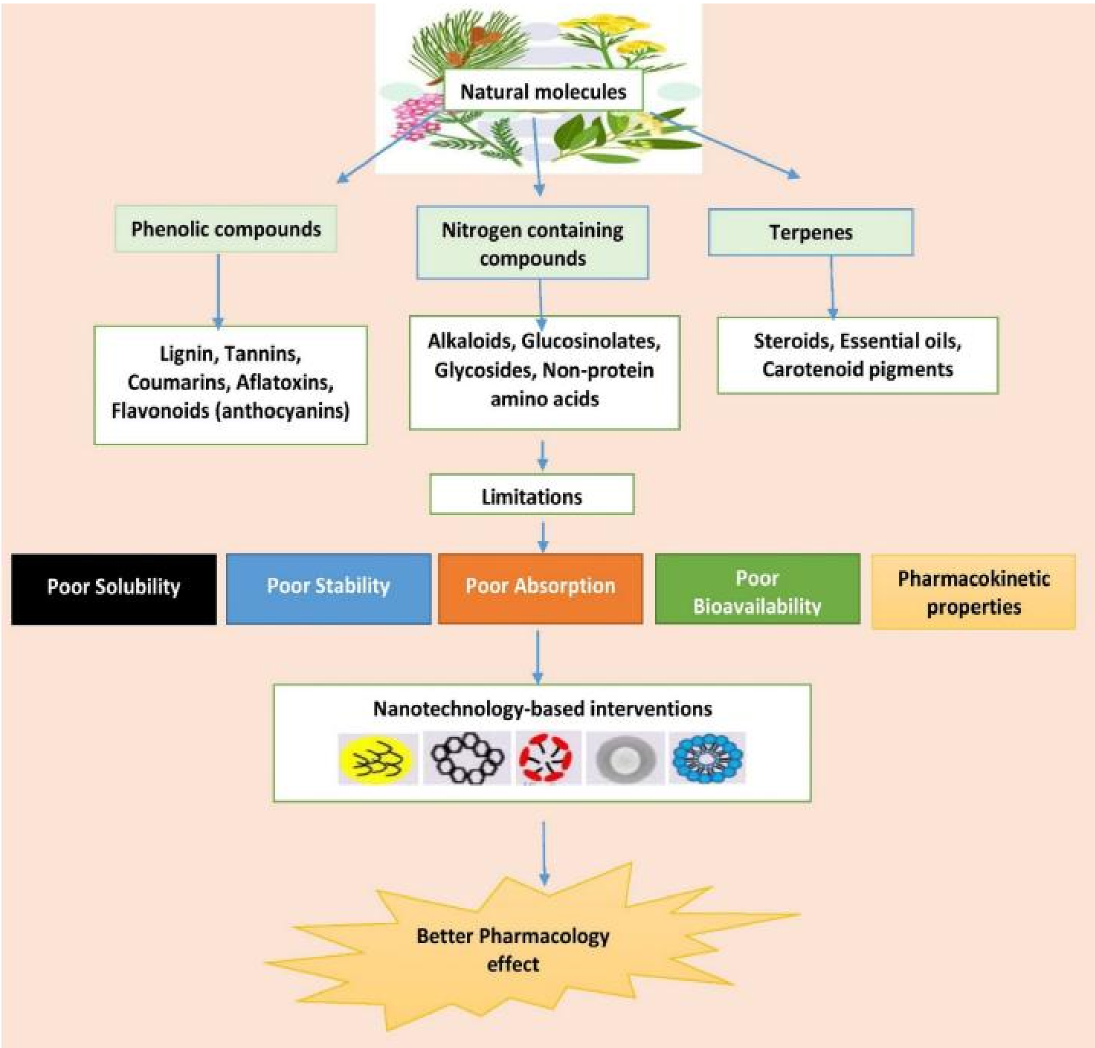


Figure 28: Nanotechnology based delivery system (Dewi et al., 2022).

II.7. Phytonanoformulations

Nanocarriers offer the flexibility of administration via various routes, including parenteral, nasal, topical, and oral delivery (Alshawwa et al., 2022). Therapeutic agents may be encapsulated within the nanocarrier matrix or attached to its surface, allowing for precise control over critical parameters such as particle size, surface charge, surface characteristics, and targeting capabilities (Alshawwa et al., 2022).

These systems can be functionalized with specific ligands to enhance cellular uptake and targeting efficiency (Alshawwa et al., 2022). Pharmaceutical nanocarriers represent a range of structures such liposomes, micelles, nanoemulsions, dendrimers, solid lipid NPs, nanospheres, nanocapsules, nanocrystals, Ethosomes and niosomes. Few nanocarriers along with phytoconstituents were depicted in (Figure 29).

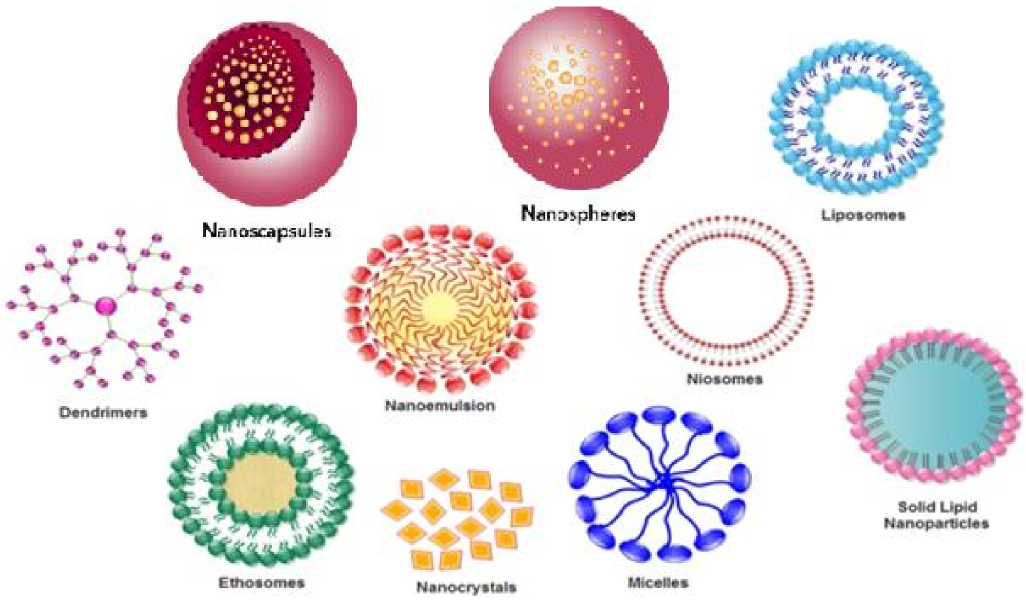


Figure 29: Few type of nanocarriers (Joudeh & link, 2022; Guadarrma-Escobar et al., 2023).

II.7.1. Micelles

Polymeric micelles composed by a co-block polymer (red and blue wavy lines). The core shell is formed encapsulating the bioactive cargo inside (Figure 30). The surface can be functionalized with linker molecules and further decorated with targeting ligands to enable targeted delivery (Vega-Vásquez et al., 2020).

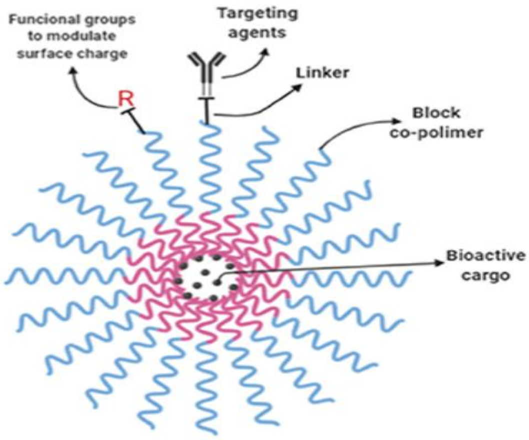


Figure 30: Schematic representation of nanomicelles (Vega-Vásquez et al., 2020).

II.7.2. Nanoemulsions

The size of the nanoemulsions ranges from10 to 200 nm (Figure 31). A nanoemulsions is adjudge to be a stable isotropic system of two immiscible liquid phases an oil phase and a water phase by means of an emulsifying agents (Shubham et al., 2018). Nanoemulsions have been utilized to incorporate essential oils and herbal extracts into food products (Farhang et al., 2025).

Nanoemulsions are efficient drug delivery systems that improve the water solubility and bioavailability of lipophilic drugs. They stabilize the drug and protect it from hydrolysis and oxidation by encapsulating it in oil droplets. They are also effective in delivering peptides vulnerable to enzymatic degradation in the gastrointestinal tract (Doe & Smith, 2022).

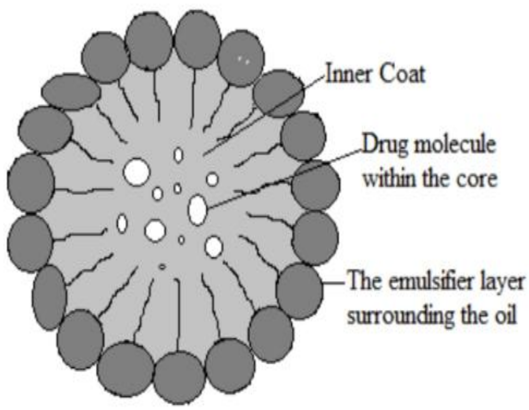


Figure 31: Schematic representation of nanoemulsions (Shubham et al., 2018).

II.7.3. Liposomes

The size of liposomes are usually between 50 and 150 nanometers (Nsairat et al., 2022). Liposome containing hydrophilic cargo in its core a hydrophobic cargo (Figure 32) allocated in the bilayer (Vega-Vásquez et al., 2020). Surface functionalization can be achieved by anchoring of targeting ligands such as antibodies and proteins (Vega-Vásquez et al., 2020).

Liposomes interact with cells through different ways, like endocytosis, fusion with the cell membrane, phagocytosis, or absorption into the membrane (Nsairat et al., 2022). Liposomes are versatile drug delivery systems that improve the solubility, stability, and bioavailability of poorly water-soluble drugs (Elingarami & Witness, 2025).

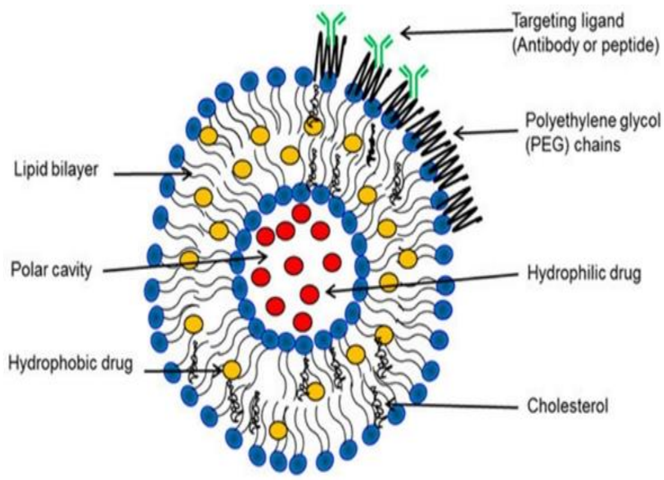


Figure 32: Schematic representation of liposomes (Fulton & Najahi, 2023).

II.7.4. Dendrimers

Dendrimers are widely studied in herbal delivery for their unique structure, including a core, interior branching, (first, second, third) generations, and terminal surface groups (Figure 33). Drugs can be attached to the terminals or encapsulated in the hydrophobic core (Jalili et al., 2023). Dendrimers structure enhances drug stability by encapsulating molecules within internal cavities and allows site-specific delivery through surface conjugation with targeting ligands (Pooja et al., 2021).

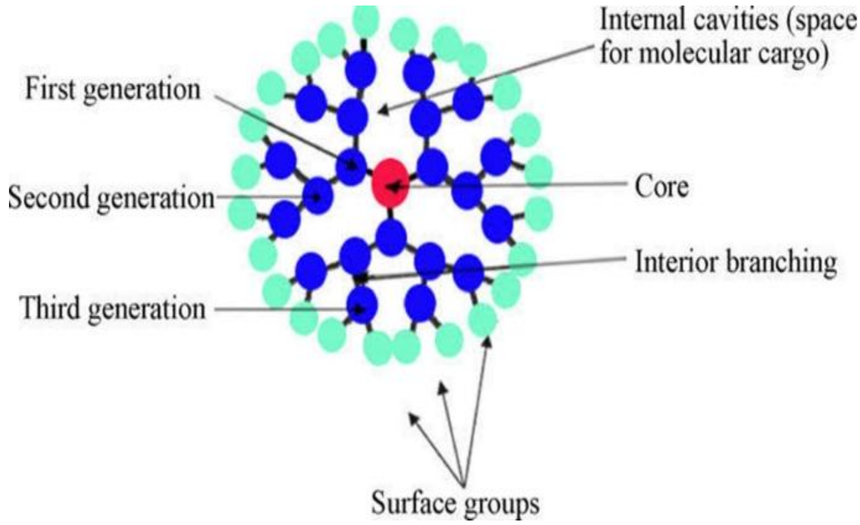


Figure 33: Schematic representation of dendrimers (Jain et al., 2010).

II.7.5. Solid lipid nanoparticles

Solid lipid nanoparticles (SLN) (Figure 34) are spherical nanoparticles. During SLN fabrication, a lipophilic bioactive cargo is dissolved in a liquid hot lipid matrix, which makes these ideal candidates for the encapsulation of lipophilic bioactive compounds (Vega-Vásquez et al., 2020).

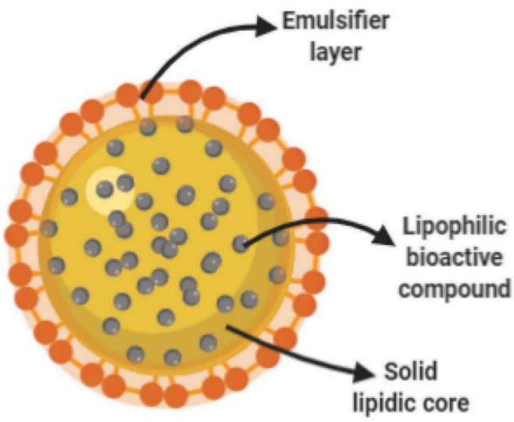


Figure 34: Schematic representation of SLN (Vega-Vásquez et al., 2020).

II.7.6. Polymeric NPs

Polymeric NPs have recently gained significant attention as drug delivery systems in phytomedicine and ranging in size from 10 to 1000 nm. NPs are generally classified into two structural types: nanospheres and nanocapsules. Nanospheres consist of a polymeric matrix in which the active compound is uniformly dispersed (Jalili et al., 2023).

Unlike nanocapsules, which have a distinct core-shell architecture (Singh et al., 2010), with the active ingredient either encapsulated within the core or adsorbed onto the polymeric membrane (Jalili et al., 2023) made from natural or synthetic polymer (Kothamasu et al., 2012). The (Figure 35) indicated the schematic representation and the constituents of nanocapsules and nanospheres.

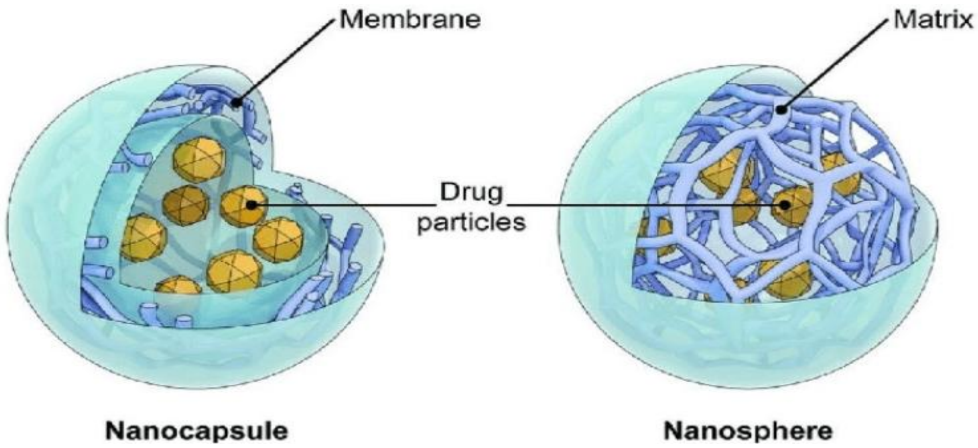


Figure 35: Schematic representation of nanocapsules and nanospheres (Atabakhshi Kashi et al., 2020).

II.7.7. Ethosomes

Ethosomes are soft, malleable structures composed of phospholipids, ethanol (20-45%), and water (Figure 36). Their unique composition allows them to penetrate deeper skin layers and facilitate greater drug permeation (Ricci et al., 2024). Furthermore, the high ethanol content of ethosomes results in being much smaller than liposomes enhances solubility of more lipophilic drugs and causes to be more flexible than liposomes (Babaei et al., 2016).

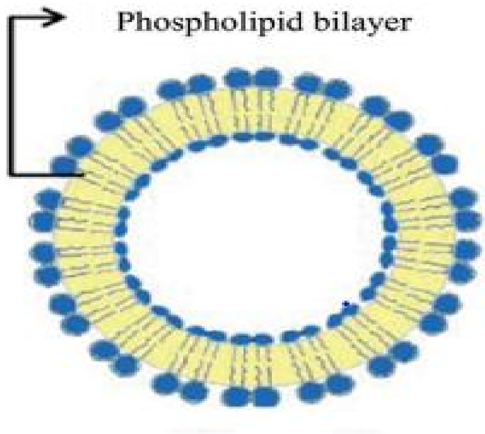


Figure 36: Schematic representation of ethosomes (Babaei et al., 2016).

II.7.8. Niosomes

The two major components utilized for the preparation of niosomes exist: lipid compounds (cholesterol or L-α-soya phosphatidylcholine) and nonionic surfactants (Figure 37). Lipid compounds are utilized to provide unbending nature, appropriate shape, and adaptation to the niosomes. The part surfactants assume the main part in the development of niosomes (Gharbavi et al., 2018).

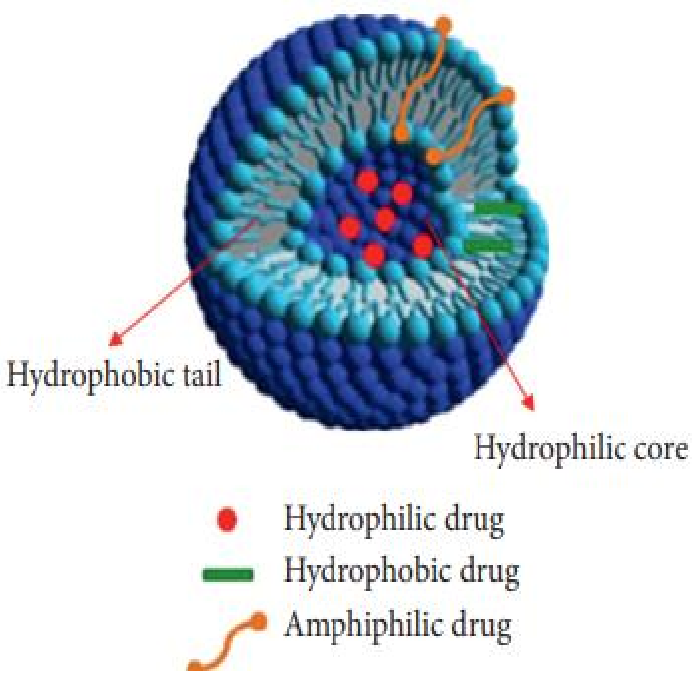


Figure 37: Schematic representation of niosomes (Gharbavi et al., 2018).

II.8. Nanotechnology based interventions

II.8.1. Benefits in drug delivery system

II.8.1.1.Bioavailability and absorption

The effective drug delivery is a key consideration in pharmaceutical development, as the plasma membrane serves as a significant barrier to cellular entry. Hydrophilic small molecule drugs, in particular, face challenges due to poor permeability, which limits their bioavailability and clinical utility (Zhang et al., 2019). Bioavailability refers to the rate and extent at which the active substance or active component is absorbed from a pharmaceutical formulation and becomes available at the site of action (Toutain et al., 2004).

In recent years, drug bioavailability has attracted attention not only during drug development but also at the early stages of drug discovery (Allam, 2011). Nanotechnology-based delivery system methods can overcome the limitations of herbal medicine, mostly by increasing their bioavailability and absorption, thereby increasing their activity (Dewi et al., 2022) and therapeutic impact of their active compounds, which often suffer from poor solubility, volatility, and limited absorption (Smith & Doe, 2024).

Absorption enhancers are functional excipients used in drug formulations to improve the uptake of active pharmaceutical ingredients by increasing their permeability across biological membranes (Aungst, 2011). The nanocarriers have garnered significant attention in drug delivery systems due to their unique nanoscale characteristics (Ding et al., 2023). Nanocarriers-based drug delivery systems offer numerous advantages such as enhanced oral bioavailability and absorption (Ding et al., 2023; Diksha et al., 2024). Polymeric micelles enhance membrane permeability, enabling them to encapsulate poorly soluble herbal medications and facilitate their absorption (Diksha et al., 2024).

Curcumin boasts numerous positive effects on the body, encompassing antioxidant, and anti-inflammatory actions. Nevertheless, its limited solubility and poor absorption in its natural state within the digestive system significantly hinder its use as a health enhancer and dietary supplement. Fortunately, recent progress in formulating curcumin at the micro and nano-scale has dramatically improved its absorption, leading to beneficial levels of active curcumin in the bloodstream. The availability of these highly absorbable forms of curcumin now facilitates a broad range of relevant investigations (Sidney et al., 2020).

Owing to their size generally between 10 and 100 nm, micelles demonstrate enhanced porosity, increased likelihood of cellular uptake via endocytosis by cells. These nanocarriers of hydrophobic chemotherapeutic agents have shown significant potential in delivering them specifically to target sites of cancer (Wahi et al., 2023).

Quercetin is a polyphenolic compound and rich in many plants, fruits, and vegetables. It exhibits anticancer activity by inhibiting growth of cancer cells and suppressing tumorigenesis and cancer progression. However, its water solubility is as low as 0.17-7.7 μg/mL and only 1% in humans and 17% in rats is bioavailable. Recently, nanomicelles have been implemented (Figure 38) to enhance the solubility, permeability, and bioavailability of quercetin for better therapeutic use (Li et al., 2022).

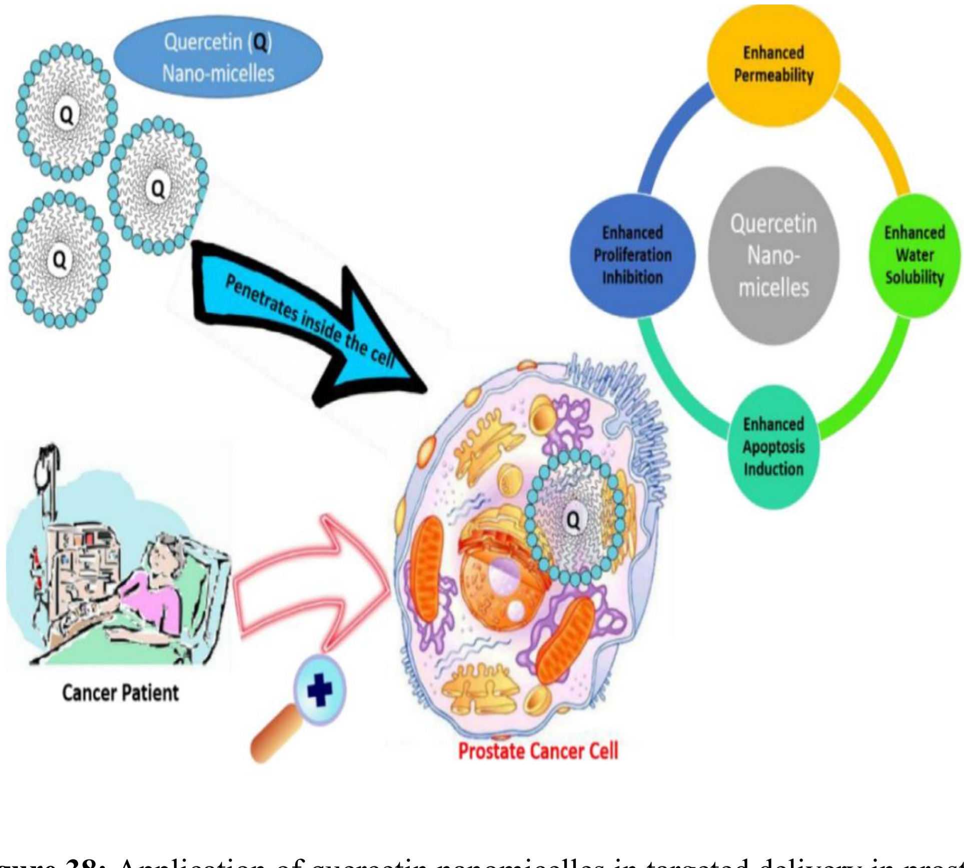


Figure 38: Application of quercetin nanomicelles in targeted delivery in prostate cancer therapy (Li et al., 2022).

II.8.1.2. Stability and controlled release

The high surface area-to-volume ratio of nanocarriers enhances the stability of drugs (Ding et al., 2023). Nanospheres and nanocapsules are typically formulated using biodegradable and biocompatible natural or synthetic polymers, enabling controlled drug release and targeted delivery to specific sites within the body (Jalili et al., 2023), Because of their small size, these nanocarriers can maximize medication delivery by ensuring that the drug reaches the affected area at the lowest effective dose, avoiding liver metabolism (Farhang et al., 2025).

II.8.2. Benefits in agriculture

Agriculture faces numerous challenges, such as reduced crop yield due to biotic and abiotic stresses, nutrient deficiency and environmental pollution (Shang et al., 2019). Recently, nanoparticles have gained significant attention for their potential agricultural applications (Figure 39) (Khan et al., 2023).

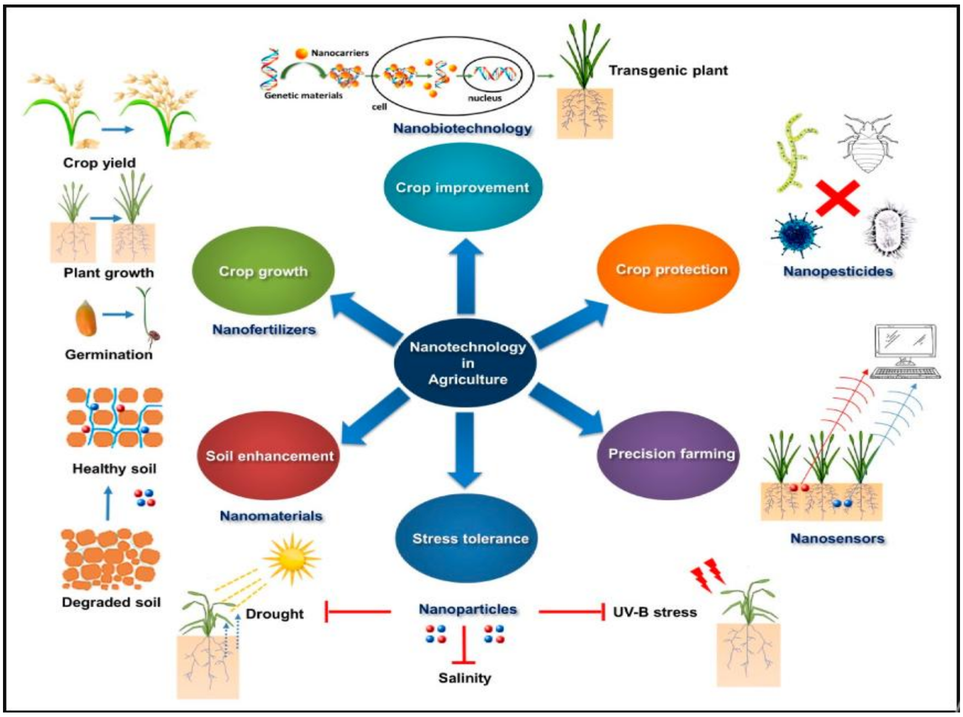


Figure 39: Nanobiotechnology in agriculture (Shang et al., 2019).

II.8.2.1. Crop growth

II.8.2.1.1. Enhanced plant growth

NMs represent a powerful and versatile tool for enhancing plant growth, development, and overall yield (Garima et al., 2020). Studies indicate that plant responses to silver NPs depend on their concentration. Furthermore, appropriate silver NPs concentrations have been shown to improve plant growth (Khan et al., 2023).

This study assessed the effects of varying concentrations (0, 50, 100, and 150 ppm) of silver NPs (Ag NPs) applied either as a foliar spray or soil drench on the growth and productivity of common bean *Phaseolus vulgaris* L. The findings revealed that a 50 ppm, low concentrations foliar spray of Ag NPs significantly enhanced vegetative growth parameter such as plant height, number of branches as well as leaf chlorophyll content. Additionally, the results suggest that of can be beneficial for enhancing the yield of *Phaseolus vulgaris* (Abo El-Nour et al., 2023).

II.8.2.1.2. Enhanced seed germination

The germination of seeds is a sensitive phase in the life cycle of plant. However, seed germination is largely affected by different parameters including environmental factors, genetic trait, moisture availability and soil fertility. In this concern, an extensive number of studies have shown that the application of NMs has positive effects on germination as well as plant growth and development (Shang et al., 2019). Seed nanopriming are a technique improve the germination, plant growth, and crop yield by helping plants resist different types of stress (Nile et al., 2022). Seed nanopriming refers to the precise application of NPs to seeds (Mahra et al., 2025).

This innovative approach (Figure 40) enhances seed germination and plant growth by stimulating key physiological processes (Mahra et al., 2025). Seed nano priming improves interactions within plant cells by enhancing electron transfer and surface reactions. This method creates tiny pores in plant shoots, improves water uptake, and activates natural defense systems using ROS. Additionally, the ROS produced act as signals that trigger protective responses and help the plant produce beneficial compounds (Nile et al., 2022).

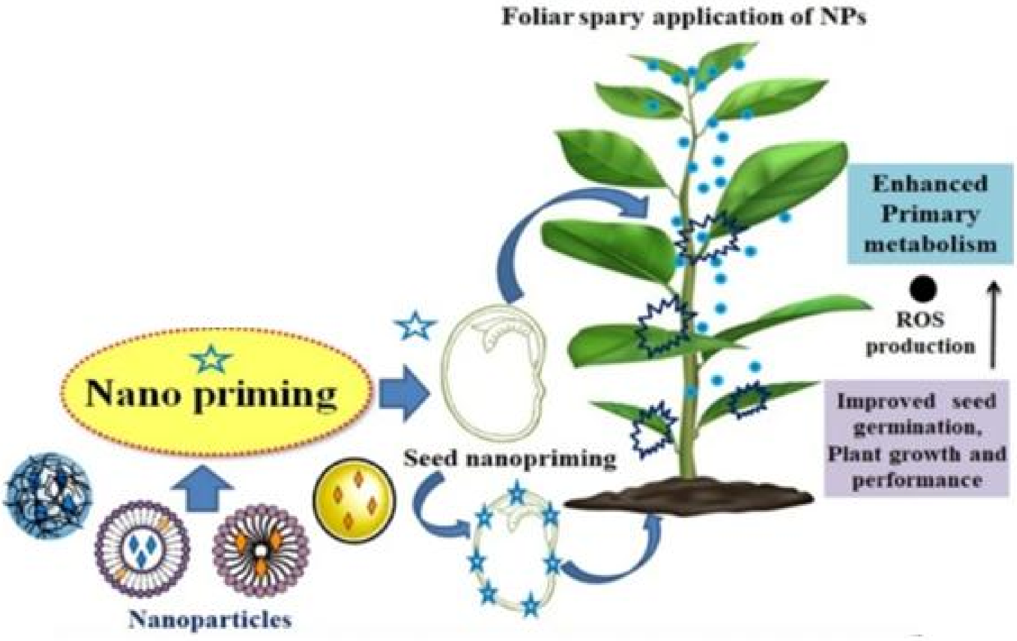


Figure 40: Seed nanopriming approach (Nile et al., 2022).

II.8.2.2. Crop nutrition

II.8.2.2.1. Nanofertilizers application

Nutrient deficiencies in food crops pose a major health issue and nanotechnology offers a promising solution through nanofertilizers. They are increasingly important in advancing sustainable agriculture (Zhang et al., 2019), as they improve nutrient uptake efficiency by delivering nutrients in a targeted (Shivam et al., 2025). The (Figure 41) indicated the advantages and the application model of nanofertilizers.

For example, conventional nitrogen fertilizers are manifested by huge losses from the soil through evaporation, or even the degradation of up to 50-70%, which ultimately reduces the efficiency of fertilizers and elevates the cost of production. On the other hand, nanoformulations of nitrogenous fertilizers prevent undesirable losses of nutrient via direct internalization by crops, and thereby avoiding the interaction of nutrients with soils, water, air and microorganisms (Shang et al., 2019).

II.8.2.3. Crops protection

II.8.2.3.1. Nanopesticides application

The assistance of nanotechnology in plant protection products has exponentially increased to achieve higher crop production. In general, conventional crop protection practices involve applications of large-scale and over-dose of fungicides, herbicides and insecticides. Among the applied pesticides, more than 90% are either lost in the environment or unable to reach the target sites essential for effective pest control (Shang et al., 2019). Nanoencapsulation of active ingredients using nanoparticles enables the slow and targeted release of chemicals like pesticides and herbicides directly to host plants (Itodo, 2019). The (Figure 41) indicated the advantages and the application model of nanopesticides.

Inorganic NPs, such as TiO_2 NPs, ZnO NPs,SiO_2 NPs and AgNPs play important roles in various arena of plant protection including microbial activity and bacterial diseases (Shang et al., 2019). TiO_2NPs , known for their safety and beneficial properties for plant protection without harming the environment (Sharma et al., 2022). ZnO NPs have recently been shown to provide effective growth control of *Fusarium graminearum*, *Penicillium expansum*, and *Aspergillus flavus* as well as pathogenic bacteria *Pseudomonas aeruginosa* (Shang et al., 2019). AgNPs are widely recognized for their strong antimicrobial effects and ability to stimulate plant growth and secondary metabolite production at suitable concentrations (Yadav et al., 2022).

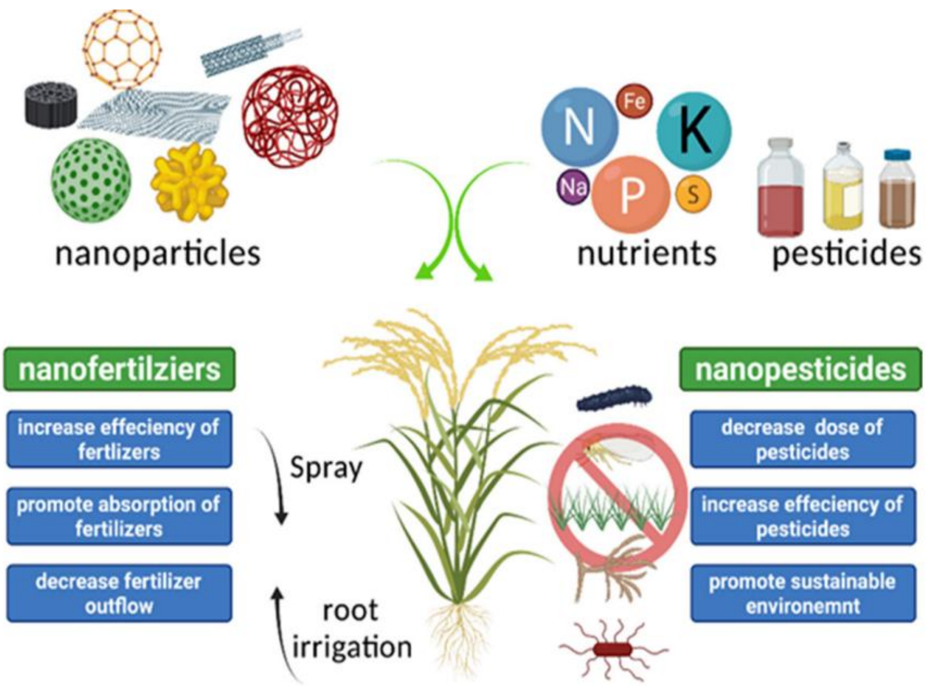


Figure 41: Advantages and the application model of nanofertilizers and nanopesticides (Liu et al., 2021).

II.8.2.4. Crop improvement

II.8.2.4.1. Nanobiotechnology

Gene transfer is an important part of genetic engineering-based plant improvement (Yadav et al., 2023) (Figure 42). Plant genetic engineering plays a vital role in enhancing crop yield and their quality (Yan et al., 2022). However, the presence of a rigid cell wall is a major hurdle for the delivery of the biomolecules in plant cells, several NMs like mesoporous silica NPs, carbon nanotubes, magnetic NPs, or MNPs have been shown to deliver nucleic acids in the plant cells (Yadav et al., 2023).

For instance, a recent study showed that conjugates of DNA and carbon nanotube were successfully transferred into multiple plant species including tobacco, cotton and wheat (Liu et al., 2021).

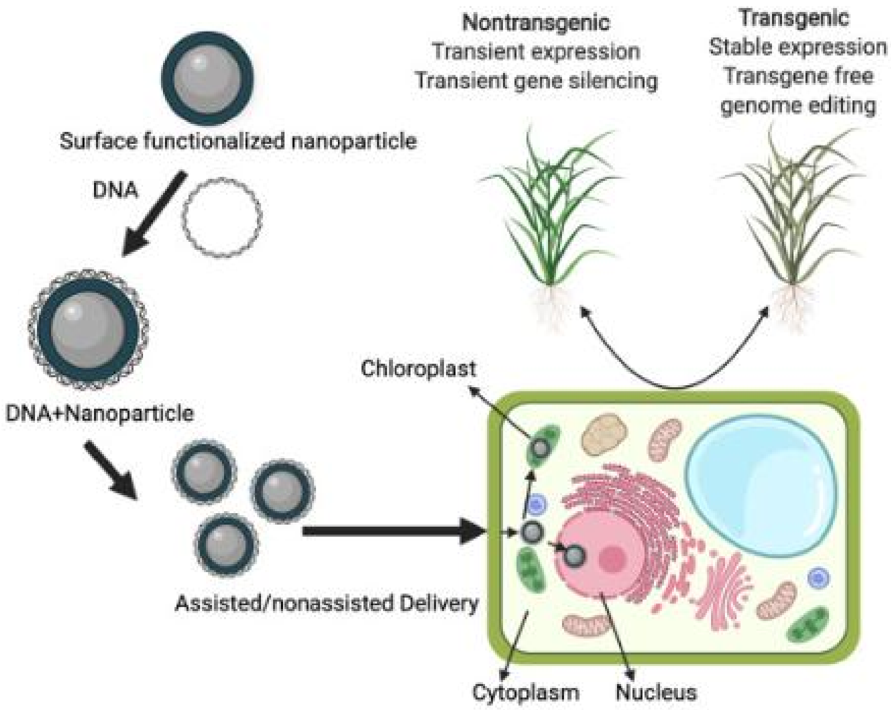


Figure 42: Genetic engineering-based plant improvement (Yadav et al., 2023)

II.8.2.5. Precision farming

II.8.2.5.1. Nanosenseurs application

Agriculture is vital to human civilization, but plant diseases caused by pathogens like bacteria, viruses, and fungi pose ongoing challenges (Yusof & Isha, 2020). Plant pathogens significantly reduce crop productivity, contributing to global food shortages for both humans and animals (Verinde et al., 2024). Nanosensors have emerged as essential tools in modern agriculture, offering early, accurate, and rapid detection of plant diseases (Figure 43). They support pathogen management and enhance traditional diagnostic methods, contributing to sustainable agriculture and improved crop productivity (Yusof & Isha, 2020) and nutritional quality by combating pathogen infections (Ashraf et al., 2025).

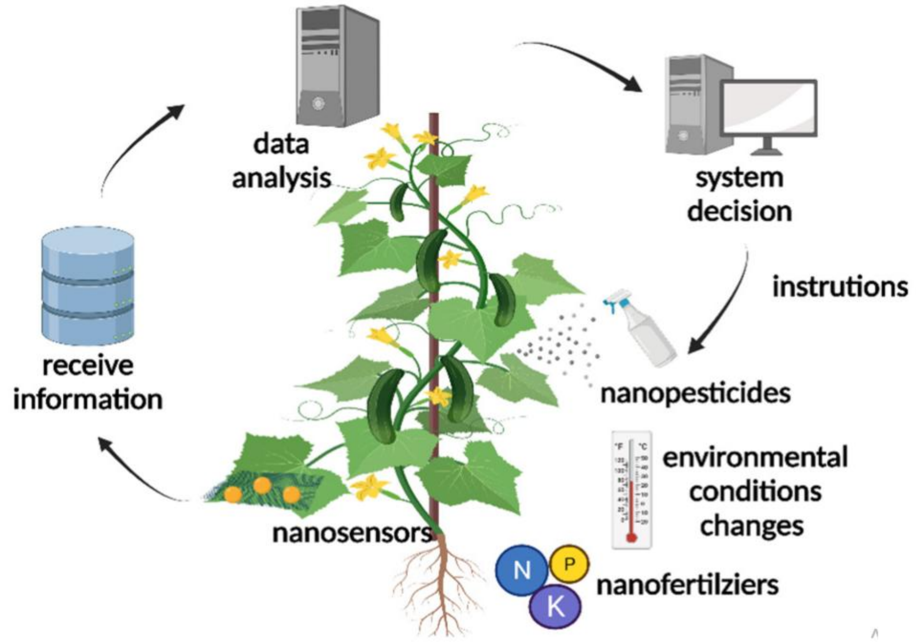


Figure 43: Applications of nanosensors in crops (Liu et al., 2021).

Tomato plants

Tomato plants are among the most widely cultivated and economically important crops globally, but their production is severely challenged by early blight disease caused by *Alternaria solani* (Ansari et al., 2023). Recently, AgNPs have gained attention for their antifungal potential. They effectively protects tomato plants from foliar pathogens (Ashraf et al., 2025).The study of (Ansari et al., 2023) evaluated the effectiveness of green-synthesized AgNPs, produced using, neem leaf extract, in promoting tomato plant growth and enhancing disease resistance (Ansari et al., 2023).

II.8.2.6. Biotic and a biotic stress tolerance

Plants employ shared signals, pathways, and triggers when responding to both living (biotic) and non-living (abiotic) stresses. This overlap can lead to cross-tolerance, where experiencing one type of stress can prime the plant's defense mechanisms, making it more resilient to other different stresses (Christine et al., 2016). (Figure 44) indicted the overview of applications of NPs in stress tolerance.

Studies show that ZnO NPs enhance drought tolerance in wheat by boosting antioxidant defenses and activating stress-related genes. Their high efficiency and low usage make ZnO NPs a sustainable option for protecting crops under drought stress (Raeisi et al., 2021). ZnO and SiO_2-NPs alleviate the harmful effects of drought by promoting higher photosynthetic rates, better stomatal conductance, increased transpiration, and improved CO_2 assimilation (Al-Selwey et al., 2023).

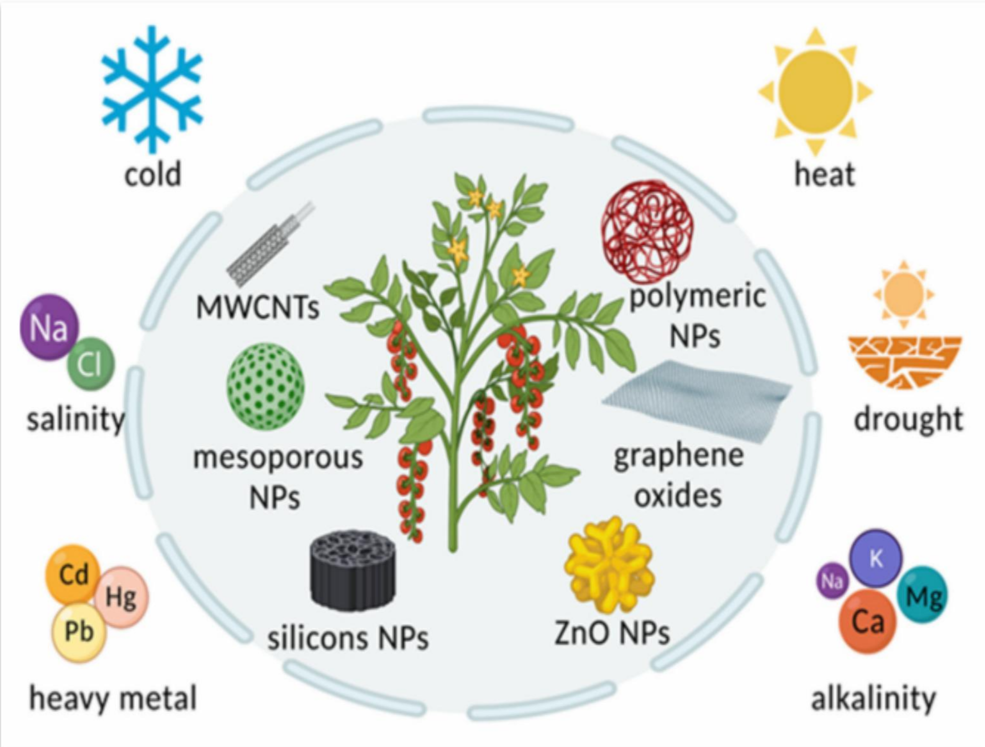


Figure 44: Overview of applications of NPs in stress tolerance (Liu et al., 2021).

II.8.2.7. Amelioration of phytosynthesis

NMs have demonstrated the ability to improve photosynthetic efficiency, highlighting their potential to revolutionize plant growth and productivity (Zaman et al., 2025). Various NPs influence plant photosynthesis. For instance, single-walled carbon nanotubes can triple photosynthetic yield in chloroplasts by accelerating electron transport and enhancing plant signaling molecules like nitric oxide. Other NPs such as SiO_2 and TiO_2 also boost photosynthesis by enhancing oxygen transport and light absorption (Poddar et al., 2020).

Chapter III
Phytosynthesis, characterization and biological activities of NPs

III.1. Phytosynthesis of NPs

NPs production involves two main approaches: top-down and bottom-up (Figure 45). The top-down and bottom-up approaches are two fundamental strategies for fabricating materials at the nanoscale. The top-down approach involves reducing the size of bulk materials down to the nanoscale through physical or mechanical means. In contrast, the bottom-up approach entails assembling larger nanostructures from individual atoms or molecules through chemical or biological processes (Abid et al., 2022). Top-down approach s relatively simple, it often results in irregularly shaped particles and lacks precise control over size and shape, which is a significant limitation (Tripathy et al., 2023). The bottom-up (or building-up) compared to the top-down method, it is generally more cost-effective, offers better scalability, and results in improved uniformity of the final product(Imran et al., 2021). Among emerging techniques, green synthesis has gained attention (Saxena et al., 2025).

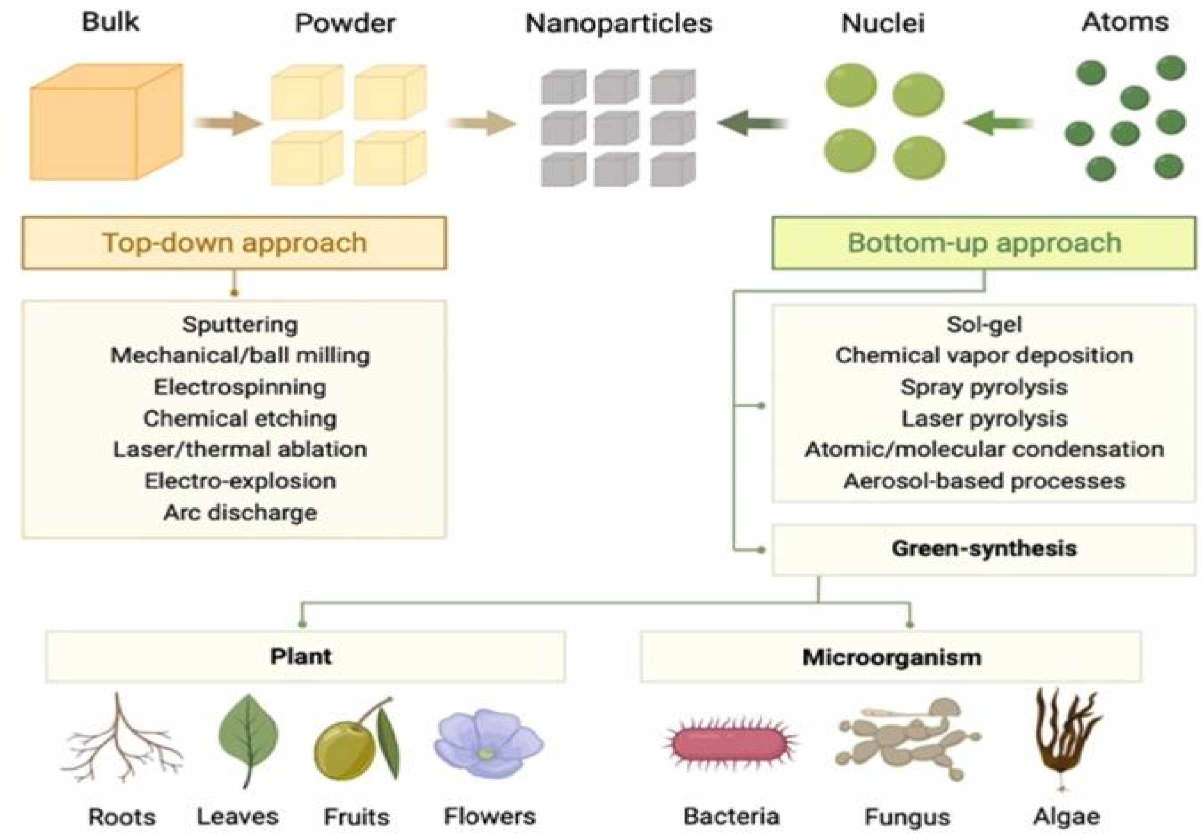


Figure 45: Top-down and bottom-up approaches to synthesising NPs (Afonso et al., 2024).

III.1.1. Green synthesis

With the increasing concern over the environmental impact of conventional chemical methods, environmentally friendly processes, commonly known as green chemistry, for the synthesis of NPs have gained growing interest in the field of nanobiotechnology (Zhang et al., 2023). Physical methods require high energy and extreme conditions, while chemical methods involve toxic, costly reagents like sodium borohydride and complex procedures. Certain advantages and potential of green synthesis are increasingly being recognized in research (Ying et al., 2022).

III.1.1.1. Sources

Biogenic NPs synthesized from natural sources have gained significant attention in recent years due to their beneficial impacts on both human health and the environment (Kulkarni et al., 2023). These nanoparticles can be produced using a variety of biological sources, including fungi, yeasts, algae, bacteria, and especially plants (Jadoun et al., 2021; Kulkarni et al., 2023). The Table V highlights biogenic NPs sources.

Table V : Sources of biogenic NPs synthesis.

Source	NPs Type	Applications	References
Bacteria	Ag, Au, ZnO	Antimicrobial agents, biosensors, wastewater treatment	Mughal et al., 2021
Fungi	Ag, Au, TiO_2	Drug delivery, catalysis, environmental applications	Mukherjee et al., 2001
Yeasts	Ag, cadmium sulfide (Cds)	Bioimaging, heavy metal detoxification	Kowshik et al., 2002
Algae	Ag, Au, iron oxide (Fe_3O_4)	Anticancer, biosorption, magnetic delivery	Chugh et al., 2021
Plants	Ag, Au, Cu	Wound healing, diagnostics, antimicrobial coatings	Iravani, 2011

III.1.1.1.1.Plants based green NPs

Medicinal plants are recognized for their rich phytochemical profiles and wide-ranging therapeutic properties. These plants species have shown considerable promise in the green synthesis of NPs for diverse applications in medicine, environmental remediation, and agriculture (Ilavenil et al., 2025). Various parts of plants including roots, stems, seeds, fruits, leaves, and flowers are widely used in the phytosynthesis of metal NPs (Figure 46) with different shapes and sizes (Tiwari et al., 2021).

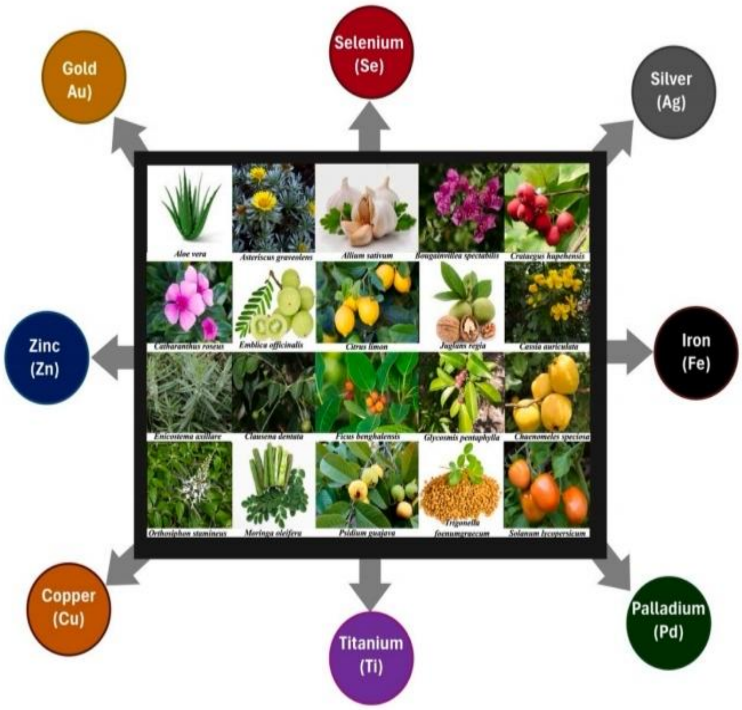


Figure 46 : Various plant parts used as sources for synthesis of metal NPs (Puri et al., 2023).

III.1.1.1.2.Biological and sustainable advantages

Plants in NPs production is emerging as a cost-effective and eco-friendly alternative to traditional chemical and physical methods for NPs production. Among biological methods, plants and their extracts are considered the most promising due to their benefits (Parveen et al., 2016)include: ecofriendliness, sustainable, biocompatible, safety, cost-effectiveness , antimicrobial effect and high yield, reducing agent, low energy and efficiency (Ulaş et al., 2025). The advantages of biogenic synthesis, emphasizing other aspects (Qamar et al., 2021; Kulkarni et al., 2023) such as variable size and shape, high stability, high surface area. The Figure 47 highlights the biological and sustainable advantages of plants-based green NPs over chemical and physical methods.

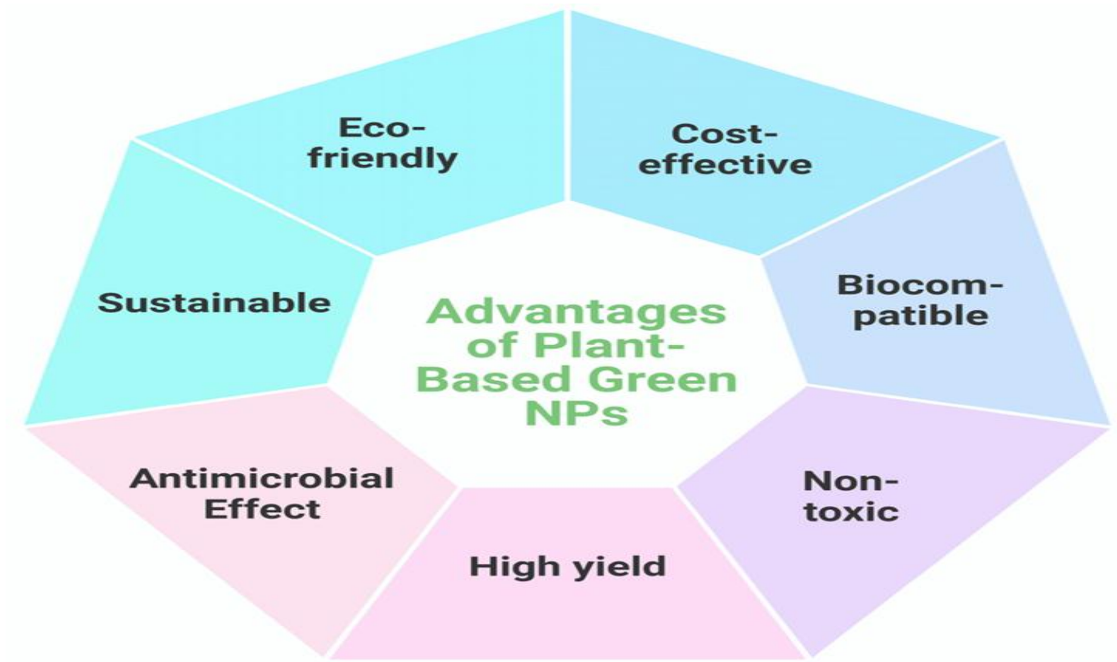


Figure 47: Biological and sustainable advantages of plants-based green NPs (Ulaş et al., 2025).

Eco-friendliness, sustainability and safety

Green synthesis is an eco-friendly approach that utilizes plant extracts rather than toxic chemicals or harsh conditions to produce NPs. It emphasizes the use of non-toxic, biocompatible materials, minimizing environmental harm and enhancing the safety of the resulting NPs for both human health and ecosystems (Madani et al., 2022; Ying et al., 2022 ; Kulkarni et al., 2023; Saxena et al., 2025).

Moreover, bio-nanotechnology profoundly influences the development of nanostructures by diminishing or eradicating pollutants (Abuzeid et al., 2023; Kulkarni et al., 2023). Plant-derived NPs provide lower environmental impact, and long-term sustainability over chemical and physical methods (Madani et al., 2022; Metha et al., 2025; Saxena et al., 2025).

Biocompatibility

The integration of nanotechnology with green chemistry forms an interdisciplinary approach that broadens the development of biologically and cytogenetically compatible metal NPs (Qamar et al., 2021).

Cost-effectiveness

Green synthesis is a cost-effective method for producing NPs (Saxena et al., 2025). These green synthesis do not require high temperatures, and pressure (Nagababu & Umamaheswara, 2016).

High yield

Green synthesis of Nps is recognized for its ability to achieve a high yield of Nps, making it both cost-effective and scalable for large-scale industrial applications (Kaur et al., 2021).

Reducing and stabilizing agent

Various plant parts including leaves, fruits, roots, stems, and seeds are commonly used, as their extracts contain phytochemicals that serve both as reducing and stabilizing agents (Jadoun et al., 2021), making them extremely useful in the synthesis of NPs with improved biological activity (Sandhu et al., 2019; Villagrán et al., 2024).

As a result, plant extracts are thought to be great candidates for the creation of metal (MNPs) and metal oxide NPs. Sugars, carboxylic acids, flavones, terpenoids, amides, ketones, and aldehydes are the primary phytochemicals found in plants that are involved in the bioreduction of NPs (Thatyana et al., 2023). The primary substances capable of reducing metal ions are shown in Figure 48 below.

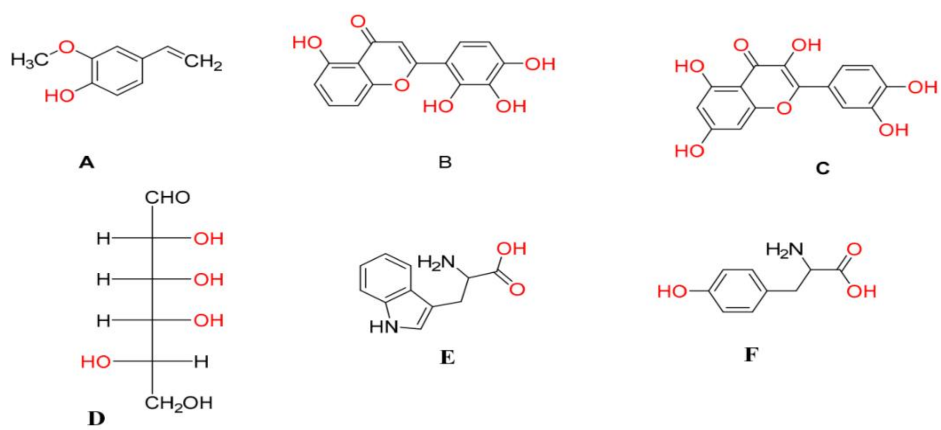


Figure 48: Types of plant metabolites involved in the synthesis of MNPs (Thatyana et al., 2023). **(A)**: terpenoids; **(B,C)**: flavonoids (luteolin, quercetin); **(D)**: a hexose with the open-chain form; **(E,F)**: amino acids (tryptophan, tyrosine).

- **Energy efficient**

These processes consume less energy, making them more sustainable(Abuzeid et al., 2023).

Energy efficiency is a pivotal advantage of green nps synthesis, as these processes consume significantly less energy compared to conventional methods, enhancing their sustainability and eco-friendliness (Abuzeid et al., 2023). While physical and chemical routes often demand harsh conditions like high temperatures or pressures, green synthesis reactions typically occur at room or relatively low temperatures without the need for energy-intensive equipment (Anand et al., 2024).

- **Efficiency**

These methods are generally less time-consuming(Kulkarni et al., 2023). The high efficiency in converting metal ions into nanoparticles, coupled with the ease of separating and purifying the final product, contributes to the increased overall quantity of nanoparticles produced (Kaur et al., 2021).

III.1.1.1.3. Phytobiosynthesis

III.1.1.1.3.1. Phytobiosynthesis procedure

The synthesis of NPs using plant-mediated reduction of metal salts is a straightforward process typically carried out at room temperature (Figure 49). The synthesis of NPs primarily requires three essential conditions: the use of an environmentally friendly solvent, an effective reducing agent, and a non-toxic stabilizing material (Villagrán et al., 2024). The extraction process involves cleaning, drying, and grinding plant material, followed by solvent extraction, commonly using water or alcohols (Zúñiga-Miranda et al., 2023).

It starts by mixing a plant extract with a metal salt solution, which immediately triggers the biochemical reduction of metal ions, often indicated by a visible color change (Zúñiga-Miranda et al., 2023). Initially, metal ions are reduced from mono- or divalent to zero-valent states, leading to the nucleation of metal atoms. As the process continues, smaller particles merge to form larger, thermodynamically stable NPs through further biological reduction. During this progression, NPs develop various shapes such as spheres, rods, cubes, and other geometries. (Shah et al., 2015).

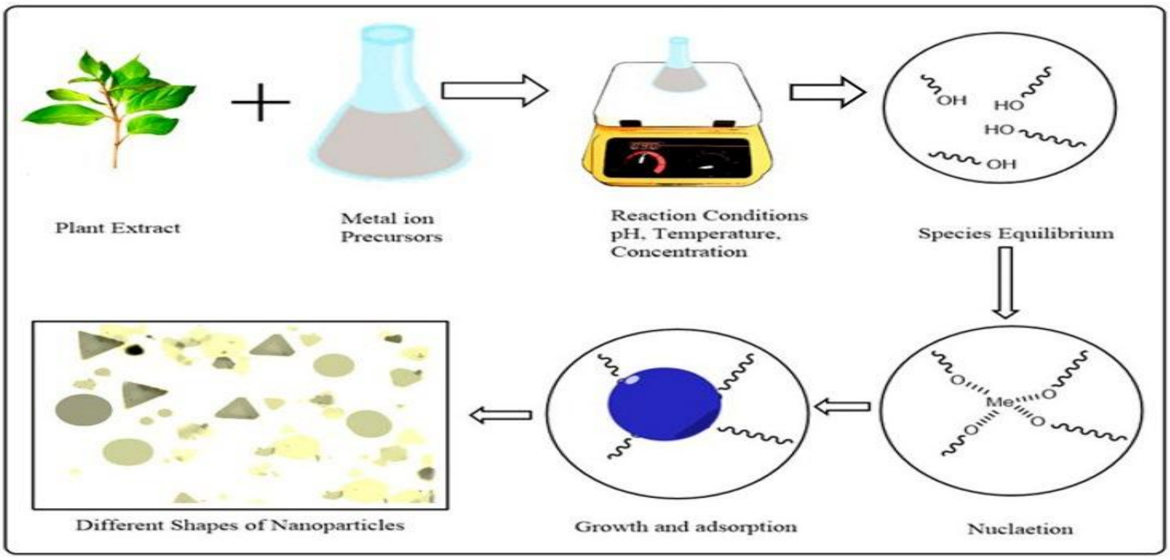


Figure 49: MNPs synthesis utilizing plant extracts. Me: metallic ion. (Bouttier et al., 2023).

III.1.1.1.3.2. Phytobiosynthesis mechanism

The mechanism of plant-mediated synthesis of metallic NPs can differ depending on various factors, including the type of plant extract, the metal salt used, reaction conditions, and the presence of bioactive components such as enzymes and antioxidants that influence both the reduction process and the properties of the resulting nanoparticles (El-Seedi et al., 2024).

In general, when metal salts are introduced to plant extracts, the biomolecules interact with metal ions through functional groups like hydroxyl. In the redox pathway, which manage this synthesis, polyphenols and other reducing agents undergo oxidation, donating electrons to metal ions and converting them from their ionic to elemental state (El-Seedi et al., 2024). Figure 50 shows metal ions binding to the stabilizing agents and reducing plant metabolites, and the ions are reduced to metal atoms.

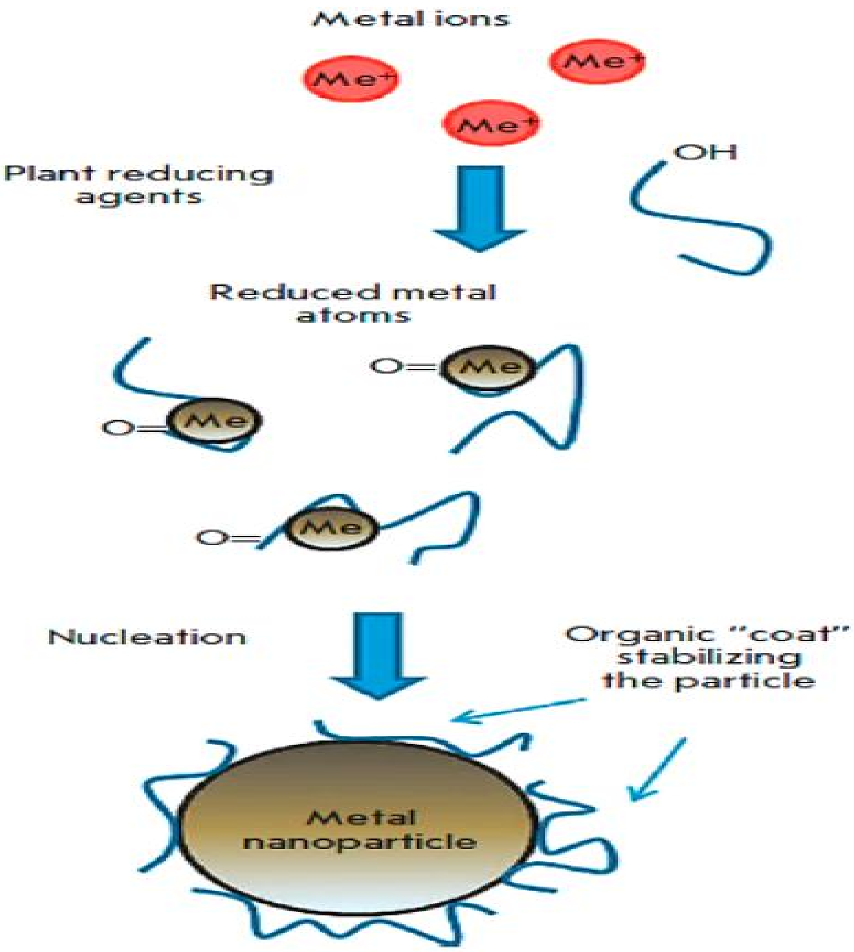


Figure 50: Mechanism of plant-mediated synthesis of MNPs (Thatyana et al., 2023).

III.1.1.1.3.3. Phytobiosynthesis fractors influencing

The synthesis of MNPs using plant extracts requires careful optimization of reaction conditions. Key parameters such as the concentration and ratio of plant extract and metal salts, pH level, reaction time, and temperature must be closely monitored and controlled (Tiwari et al., 2021; Azad et al., 2023). Ultimately, the plant extract stabilizes the nanoparticles, and factors like metal salt levels, pH, reaction time, and temperature significantly influence their final size, shape, and quality (Shah et al., 2015; Zúñiga-Miranda et al., 2023). Certains impacts of these facteurs affecting synthesis of NPs are indicated in Figure 51.

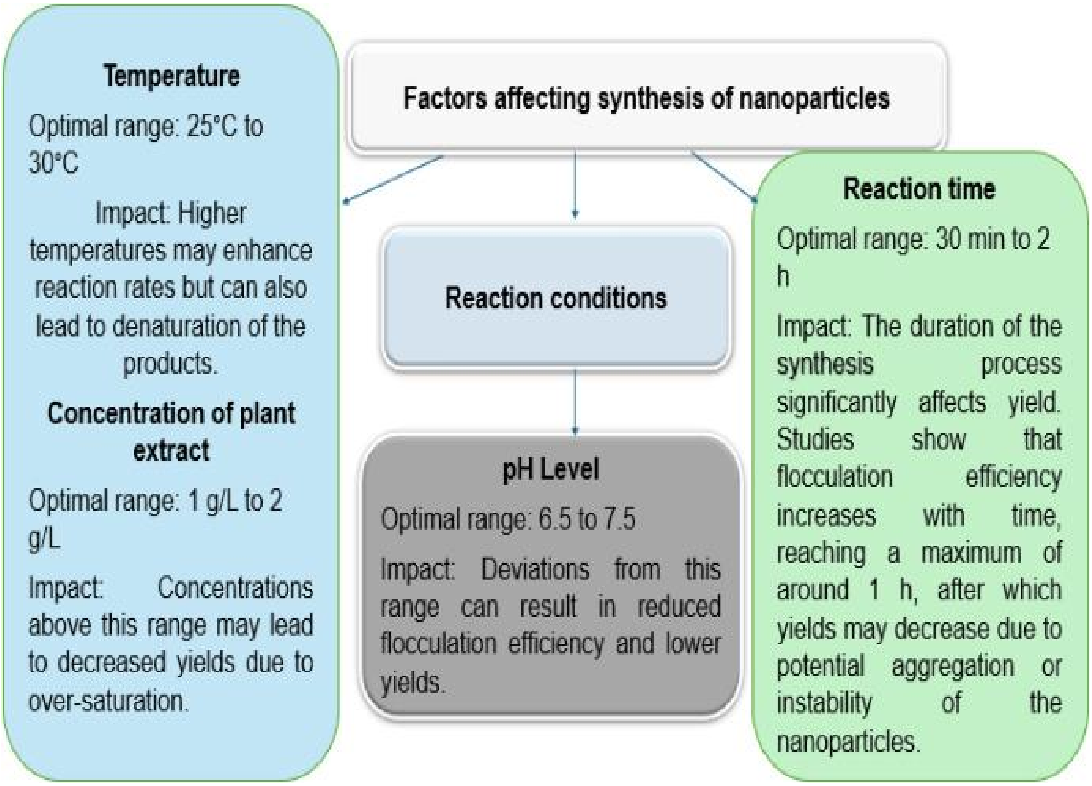


Figure 51 :Factors affecting the synthesis of iron NPs (Nkanyiso et al., 2025).

pH

pH plays a critical role in the green synthesis of NPs, significantly affecting their formation. Studies have shown that the pH of the reaction medium influences both the size and morphology of the resulting NPs. By adjusting the pH, researchers can effectively regulate NPs dimensions. This impact has been particularly evident in the synthesis of silver NPs, where variations in pH have been shown to alter their shape and size (Patra et al., 2014).

Temperature

Higher reaction temperatures generally lead to the formation of smaller NPs due to faster ion reduction and enhanced nucleation. In contrast, lower temperatures result in larger particles as they favor growth over nucleation. For example, silver NPs synthesized with olive leaf extract became smaller with increased temperature (Hongyu et al., 2020).

III.2. Characterization methods

NPs exhibit unique chemical and physical properties due to their nanoscale dimensions and high surface area. Their reactivity, and other characteristics are influenced by their shape, size, and structure (Khan et al., 2021). Therefore, the physicochemical characterization of synthesized NPs is critically important before its application in various sectors (Dikshit et al., 2021).

NPs are characterized using a variety of techniques (Figure 52) for analyzing various characteristics (Singh et al., 2023) such as size, shape, surface morphology, surface area, structure, stability, elemental and mineral decomposition, homogeneity, intensity and others, which will provide important information about the NPs, which subsequently determined their end-use applications. Additionally, the electrical and thermal conductivity and purity of NPs can also be obtained by using these techniques (Dikshit et al., 2021).

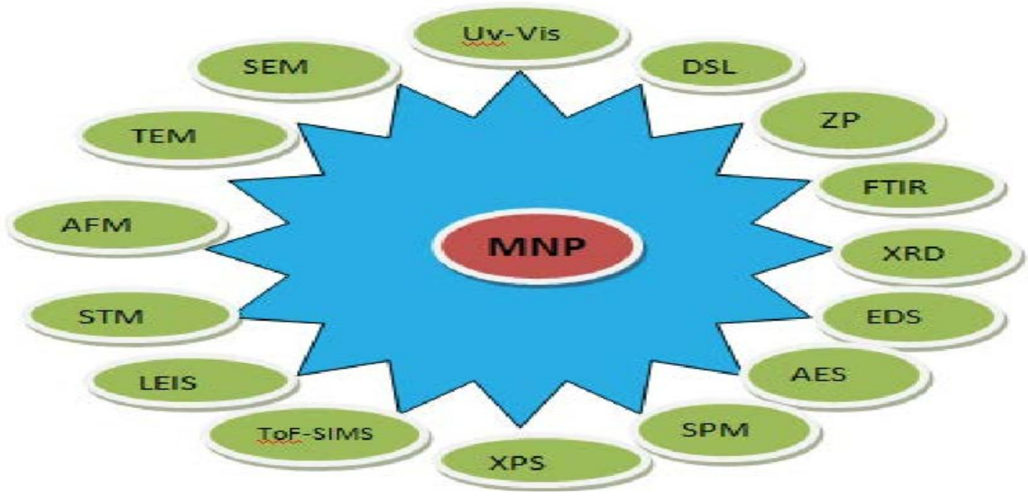


Figure 52: Summary of characterization techniques of MNPs (Kiranmai & Ramesh, 2017).

UV-Vis: Ultraviolet-visible spectroscopy; **DLS:**Dynamic Light Scattering; **ZP:** Zeta Potential; **FTIR:** Fourier-Transform Infrared Spectroscopy; **XRD:** X-ray Diffraction; **EDS:** Energy-Dispersive X-ray Spectroscopy; **AES:** Auger Electron Spectroscopy; **SPM:** Scanning Prob Microscopy; **XPS:** X-ray Photoelectron Spectroscopy; **TOF-SIMS:** Time-of-Flight Secondary Ion Mass Spectrometry; **LEIS:** Low-Energy Ion Scattering; **STM:** Scanning Tunneling Microscopy; **AFM:** Atomic Force Microscopy; **TEM:** Transmission Electron Microscopy; **SEM:** Scanning Electron Microscopy.

III.2.1. UV-Visible Spectroscopy

Visible (UV-Vis) spectroscopy is a widely used analytical technique for characterizing NPs, particularly noble MNPs like Ag and Au (Mourdikoudis et al., 2018). This method is is, based on the principle of surface plaque resonance (SPR) (Roy et al., 2021). For instance, in the synthesis of AgNPs, UV-Vis spectroscopy can reveal a characteristic SPR absorption band around 414 nm, which confirms the successful formation of spherical Ag NP. Therefore, UV-

Vis spectroscopy serves as a rapid and non-destructive tool for assessing the optical properties and stability of NPs during and after synthesis (Mourdikoudis et al., 2018).

III.2.2. Dynamic Scattering Light

Dynamic Light Scattering (DSL) is a technique used to determine the diameter of various particles dispersed in a liquid medium. These particles may be organic such as polymers, carbohydrates and proteins or inorganic, including metals like Au, Ag and transition metal oxides (Ramos, 2017). DSL can also used to measure nanoparticles size (Roy et al., 2021).

III.2.3. Zeta Potential Analysis

Zeta Potential (ZP) analysis is a standard method used to determine the surface charge and assess the colloidal stability of NPs formulations. In this technique, the velocity of NPs under an applied electric field is measured to evaluate their movement toward electrodes. (Jain et al., 2021).

III.2.4. Fourier Transform Infrared Spectroscopy

FTIR (Fourier-Transform Infrared) spectroscopy identifies functional groups present in the sample (Roy et al., 2021) on the NPs surface and confirms the involvement of biomolecules in capping and stabilization. FTIR spectroscopy facilitates the identification of compounds based on their absorption spectra (Pasieczna-Patkowska et al., 2025).

III.2.5. X-Ray Diffraction

X-Ray Diffraction (XRD) is a non-destructive analytical technique used to investigate the atomic and molecular structure of materials by analyzing the scattering patterns of X-rays. It offers essential insights into a material’s phases (Hamza & singh, 2025), crystal structure (Roy et al., 2021), average crystallite size, strain, orientation, texture, and defects. XRD is extensively used in NMs research for structural characterization (Hamza & singh, 2025).

III.2.6. Energy-dispersive X-ray spectroscopy

Energy-Dispersive X-ray Spectroscopy (EDX) has rapidly evolved, particularly in combination with scanning transmission electron microscopy (STEM), enabling atomic-resolution mapping of elements in nanostructures. This technique provides semi-qualitative and quantitative data, useful in many fields such as biology, medicine, pharmacology (for tracking the distribution of nanoparticles or drugs), as well as in environmental analysis and the study of mineral accumulation in tissues (Jagadeesh et al., 2024).

III.2.7. Scanning Probe Microscopy

Scanning Probe Microscopy (SPM) can be employed not only to determine particle size but also to assess their mechanical properties. Both dimensional and mechanical measurements at the nanometer scale necessitate robust traceability methods to ensure the comparability and reproducibility of results. Consequently, it is crucial to evaluate the measurement uncertainty, as it significantly influences the reliability and credibility of the obtained data (Feltin et al., 2020).

III.2.8. Atomic Force Microscopy

Characterization of nanoparticles based on size, morphology, and surface charge was performed using atomic force microscopy (AFM), scanning electron microscopy, and transmission electron microscopy(Mourdikoudis et al., 2018).

III.2.9. Scanning Electron Microscopy and Transmission Electron Microscopy

To investigate the crystal structure and morphology of NPs, a combination of Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) was employed. TEM provided detailed information on NPs size, shape, crystallographic orientation, and structural defects and geometric phase analysis. SEM, which offers three-dimensional shape information (Neumann & Rafaja, 2024).

III.3. Biological activities of NPs

III.3.1. Phytosynthesis antibacterial NPs

Green-synthesized AgNPs, exhibit broad-spectrum antibacterial activity against a variety of bacteria. This potent action is primarily attributed to their high surface-area-to-volume ratio, which allows for effective interaction with microbial cells (BalaKumaran et al., 2024). Once bacteria penetrate the bacterial membrane, NPs interfere with vital cellular components such as cell membrane, mitochondria, DNA, enzymes, and ribosomes (Wang et al., 2017) generating ROS that cause oxidative stress, and interfering with essential cellular DNA and proteins (Kaur et al., 2021; Abuzar et al., 2023). These interference between NPs and bacteria results also membrane disruption, and changes in gene activity (Wang et al., 2017). The Figure 53 showed certain antibacterial mechanisms of AgNPs.

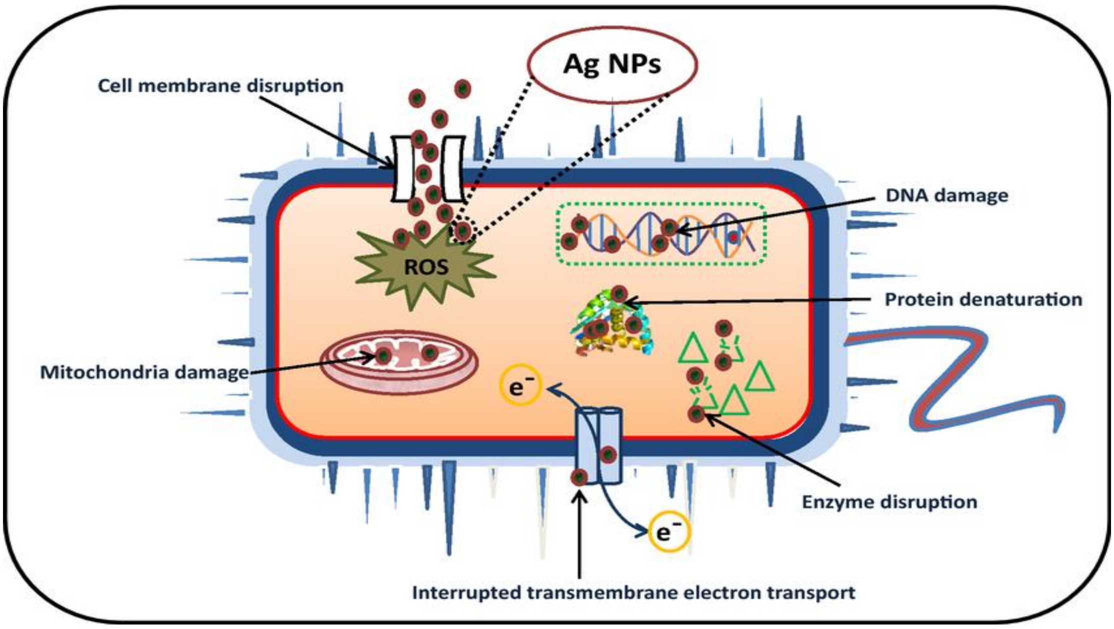


Figure 53: Mechanism of antibacterial activity (Yaqoob et al., 2020).

III.3.2. Phytosynthesis antiviral NPs

Due to their nanoscale dimensions, NPs exhibit notable antiviral properties. NPs directly enter into the host cell besides the direct interaction with viral surface glycoproteins and exert their antiviral activity through binding to viral and thereby blocking the viral replication mechanism inside host cells (Sharmin et al., 2021). NPs exhibit others diverse antiviral mechanisms such as virus genomes binding, receptor blocking and disrupting viral proteins (Bhatti & DeLong., 2023). The Figure 54 showed certain antiviral mechanisms of AgNPs.

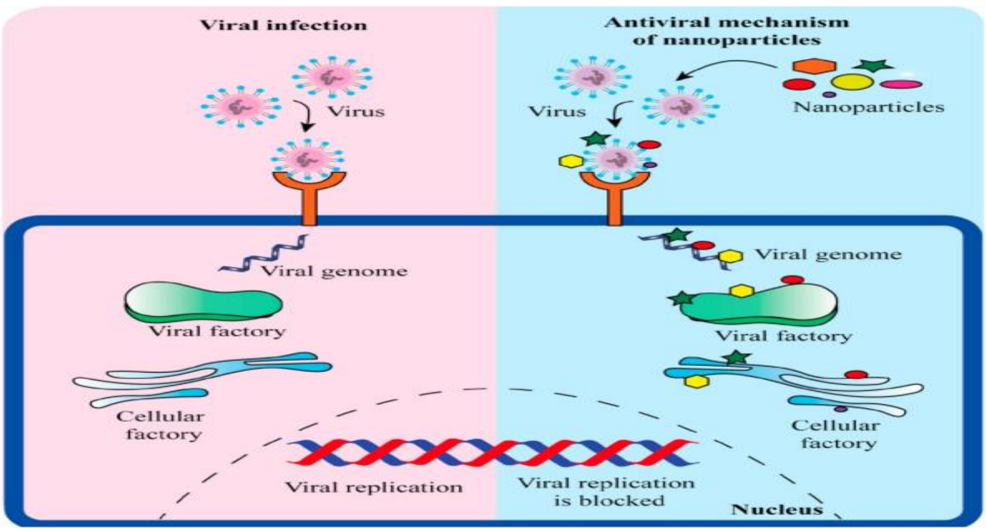


Figure 54: Schematic representations of the antiviral mechanism of NPs (Sharmin et al., 2021**).**

Antiviral activity of NPs as demonstrated by iron oxide NPs altering the RNA transcription of the influenza virus and zinc oxide NPs inhibiting its cell proliferation. AgNPs have shown strong antiviral activity against viruses by binding to viral particles and blocking their replication (Sharmin et al., 2021). Quantum dots and polymeric NPs can block viral entry by altering surface proteins or receptors (Bhatti &DeLong., 2023). The Table VI indicated the synthesis of antiviral NPs using various plant product.

Table VI: Synthesis of antiviral NPs using various plant products

Plant	Metal	Target virus	Reference
Azadirachta indica **(Neem)**	Ag	Herpes simplex virus	(Ghosh et al., 2012)
Camellia sinensis **(Green tea)**	Au	Influenza A virus	(Song et al., 2011)
Zingiber officinale **(Ginger)**	Ag	Chikungunya virus	(Balasubramanian et al., 2021)
Allium sativum **(Garlic)**	Se	Human immunodeficiency virus	(Khiralla & El-Deeb, 2015)
Ocimum sanctum **(Holy basil)**	Ag	hepatitis B virus.	(Rajakumar et al., 2012)

III.3.3. Phytosynthesis anticancer NPs

Recent progress in nanoparticle-based drug delivery systems has significantly mitigated the limitations associated with conventional cancer treatments. These advanced systems offer the advantages of targeted delivery, controlled drug release, and improved therapeutic efficacy (Sharmin et al., 2021). AuNPs derived from plants have shown promising results in targeting cancer cells; their selective toxicity and enhanced permeability effect make them effective in inhibiting cancer cell growth (Nawaz et al., 2024).

Additionally, the metal oxide NPs are extensively applied in cancer therapy. Cerium oxide (CeO_2) and ZnO NPs are synthesized using *Rubia cordifolia* L leaf extracts through a green synthesis method. These NPs showed significant anti-proliferative effects approximately against osteosarcoma cells, primarily by inducing high levels of ROS (Jeevanandam et al., 2020). The Figure 55 indicated phytosynthesized anticancer of NPs.

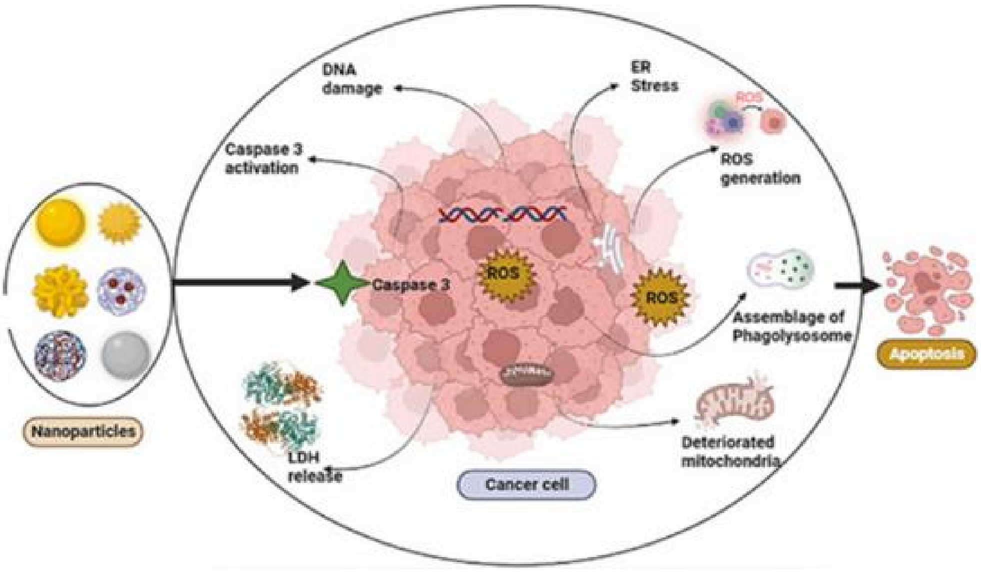


Figure 55: Schematic representation of the anticancer activity of NPs (Radulescu et al., 2023).

III.3.4. Phytosynthesis antioxidant NPs

The green-synthesized NPs exhibit significant antioxidant potential. For instance, *Hibiscus rosa-sinensis* effectively synthesized copper Cu NPs at optimal temperatures, which showed strong antioxidant activity in hydrogen peroxide assays. Similarly, Cu NPs derived from plant tubers demonstrated notable scavenging activity against DPPH, nitric oxide, and superoxide radicals, highlighting their role in preventing oxidative stress a key factor in the progression of various diseases (Balkrishna et al., 2021).

NMs possessing enzyme-like activity, termed nanozymes, have attracted considerable interest due to their advantages over their natural counterparts. Cu, Mg, Fe, Ce, Co, Au, and other metals are suitable for the preparation and testing of nanozymes. These MNPs have demonstrated effectiveness as superoxide dismutase (SOD), catalase (CAT), glutahation peroxidase (GPx) and other enzyme-like agents (Jomova et al., 2024). Nanozymes such as CeO_2 NPs exhibit CAT-like activity by breaking down hydrogen peroxide (H_2O_2) into water and oxygen (O_2), thereby protecting cells from oxidative damage. For SOD-like activity, nanozymes made from transition metals such as Ce, Cu, and Fe catalyze the dismutation of superoxide radicals (O_2^-) into H_2O_2 and O_2. Regarding GPx-like activity, nanozymes use glutathione to reduce H_2O_2, (Thao et al., 2023). The Figure 56 illustrate the CAT like and SOD like of nanozymes.

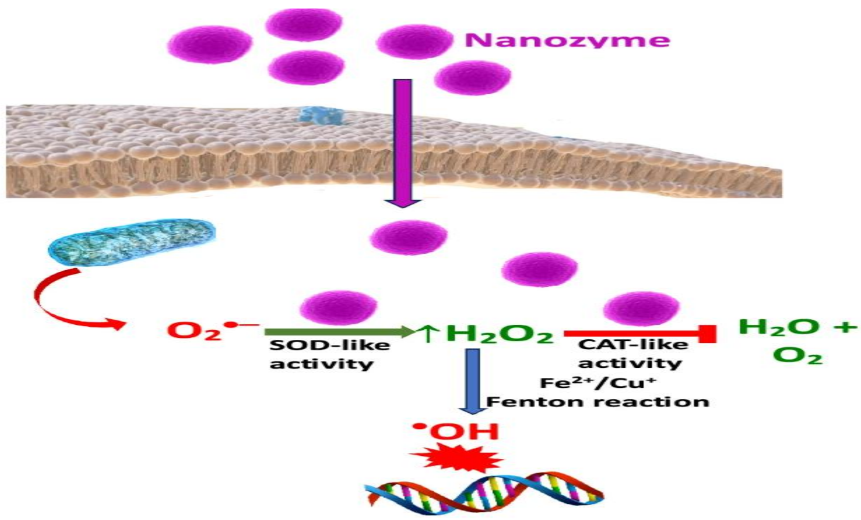


Figure 56: CAT-like activity and SOD-like activity of nanozymes (Jomova et al., 2024).

III.3.5. Phytosynthesis anti-inflammatory NPs

Biogenic MNPs have shown anti-inflammatory potential by suppressing or reducing the pro-inflammatory cytokines (Gonfa et al., 2023). Au NPs inhibit the production of key pro-inflammatory cytokines such as Interleukin-1 beta (IL-1β), Interleukin 6 (IL-6), Interleukin 8 (IL-8), and Tumor Necrosis Factor alpha (TNF-α) in macrophages treated with lipopolysaccharides (Agarwal et al., 2019). The Figure 57 highlights the mechanism of AuNPs to reduce the expression of pro-inflammatory cytokines.

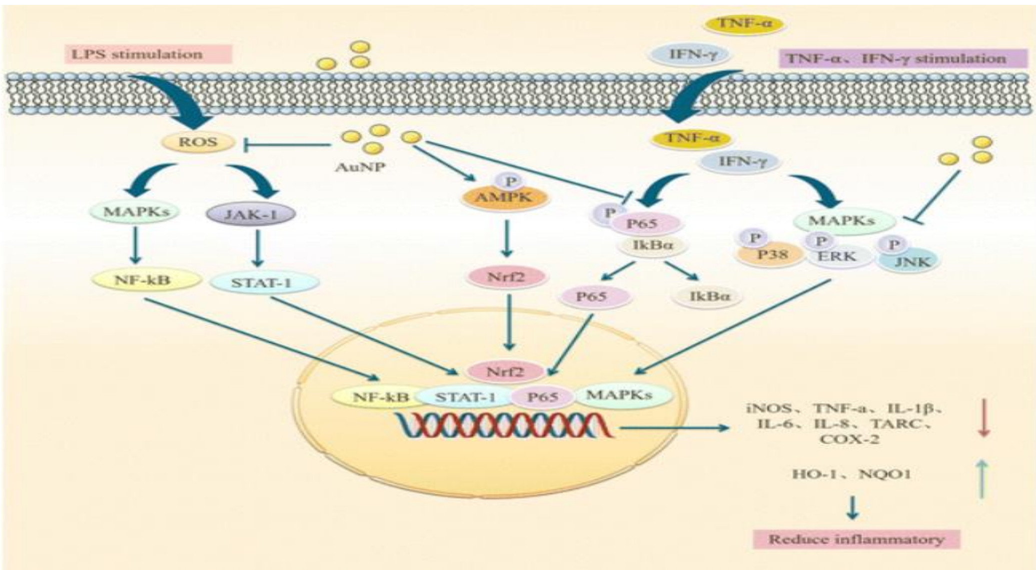


Figure 57: Mechanism of AuNPs to reduce the expression of pro-inflammatory cytokines (Aili et al., 2023).

III.3.6. Phytosynthesis anti-diabetic NPs

Minerals such as Zn, in particular, is vital for the synthesis and secretion of insulin. ZnONPs have shown significant antidiabetic potential by enhancing insulin activity (Figure 58). Additionally, CeO_2 NPs help protect pancreatic β-cells from oxidative stress and AuNPs regulate blood glucose and reduce ROS production. Natural phenolic compounds such as catechins and rosmarinic acid especially in NPs form have also proven effective in inhibiting the α-glucosidase enzyme, slowing carbohydrate digestion and reducing blood glucose (Debele & Park., 2022).

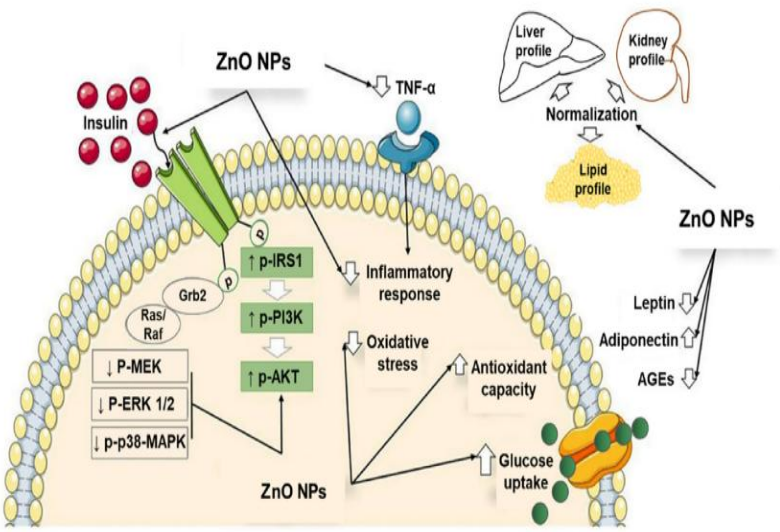


Figure 58: Mechanism of ZnONPs to reduce blood glucose (Ruifang et al., 2023).

Conclusion

Conclusion

It is clear that there is an immense need to develop methods or technologies that allow us to cope with the contrasting challenges. The use of nanomaterials for targeted drug delivery has also dramatically progressed with exceptional applications to reduce the limitations of conventional drug delivery systems. Most challenges with drug delivery, such as low water solubility, poor bioavailability, poor pharmacokinetic profile and poor bioactivity of different active natural molecules present in plant, can be solved using nanotechnology. Therefore, the development of herbal medicines with nanotechnology-based delivery systems might be an alternative strategy for increasing their pharmacological activity.

In addition, nanoparticles can overcome various others physiological obstacles; they have properties that reducing dose frequency, as well as enhancing distribution time and deliver the drug to the target site in a nonspecific, through either enhanced permeability or specific, through binding specific target receptors manner. Direct delivery of the drug to the site of action can minimize systemic toxicity while also increasing drug concentration at the target site

Likewise, the rapid growth of the population, deterioration of the environment, climate changes, traditional agriculture and global agricultural systems are facing numerous, unprecedented challenges. Increased use of nanotechnology could provide innovative solutions to improve sustainable agriculture, exhibit great potential for improving the environment and increasing the production and quality of crop plants, which would also fulfill food demands.

Current studies have shown that nanotechnology can be widely used to address various agricultural problems, such as nanofertilizers and nanopesticides use, and plant stress induced by extreme climate. Besides, nanomaterials significantly promote plant growth, seed germination, stress tolerance, nanosensors, and nanobiotechnology including, rapid and simple genome modification and transgene expression in intact plant cells. Due to their direct and intended applications in the precise management and control of efficiency of these inputs (fertilizers, pesticides, herbicides), nanotools, such as nanobiosensors, support the development of high-tech agricultural farms and minimizing relevant losses. The integration of nanotechnology into nanosensors has greatly increased their potential to sense and identify the environmental conditions or deficiencies. As well, we also should find an economical point of application of NMs that balance crop production and environmental protection .

However, in addition to the positive aspects of nanotechnology, there are still many negative aspects huge gaps such as the ecotoxicity of different NMs towards the environment and the organisms present in the ecosystem. In the same way, engineered NPs represent a toxicological damage including reactive oxygen species generation, protein misfolding, membrane perturbation and direct physical damage. Therefore, further researchs are urgently needed to develop a regulatory framework based on objective scientific research, which will limit human exposure to unwanted engineered nanomaterials in the environment to safe levels. However, the therapeutic use of nanomaterials in medicine requires a different framework, which balances the therapeutic benefit against the potential risk of harm .

In conclusion, integrating nanotechnology with herbal medicine could revolutionize healthcare by making traditional remedies more effective, precise, and scientifically validated. Ongoing collaboration among experts will be key to advancing this innovative field.

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