Green Synthesis of Cu and TiO_2 NPs using Plant Extracts: Antimicrobial and Biomedical Perspectives

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Summary: The rapid advancement of nanotechnology has revolutionized the use of metal and metal oxide nanoparticles in biomedical and environmental applications. Among these, copper (Cu) and titanium dioxide (TiO_2) nanoparticles have received increasing attention due to their low cost, biocompatibility, and eco-friendly synthesis potential. While various chemical and physical synthesis routes exist, green synthesis has emerged as a sustainable and non-toxic alternative owing to its simplicity, reliability, and minimal environmental impact. This review presents a consolidated discussion of plant-mediated green synthesis of Cu and TiO_2 nanoparticles, integrating synthesis mechanisms, structural characteristics, and broad-spectrum antimicrobial performance. The paper uniquely bridges the relationship between plant phytochemicals, nanoparticle morphology, and therapeutic efficacy, revealing how plant-mediated synthesis directly influences antimicrobial, antifungal, antiviral, anticancer, and antioxidant behaviors. This review paper presents an integrative perspective, consolidating current understanding of Cu and TiO_2 nanoparticles as next-generation, multifunctional, and sustainable nanomaterials for biomedical and therapeutic applications.

Key words: Green Synthesis; Metal NPs; Antibacterial activity; Plant extracts; Cu@TiO_2 NPs

Introduction

A well renowned physicist, Richard Feynman, delivered a seminal lecture titled *"there are plenty of rooms at the bottom: an invitation to dive into the new field of physics"* at the annual American Physical Society meeting at Caltech. In his talk, R. Feynman explored the possibility of directly manipulating individual atoms, proposing it as a more advanced form of synthetic chemistry than the methods available at the time. Although versions of his lecture were published in popular magazines, it remained largely unnoticed until the 1980s [1]. Building on Feynman's ideas, K. Eric Drexler introduced the concept of self-replicating "*billion tiny factories*" in his 1986 book *Engines of Creation: The Coming Era of Nanotechnology*, emphasizing computer-controlled nano-processes rather than human operation [2]. In 1991, *Drexler, Peterson,* and *Pergamit* further expanded these ideas in *Unbounding the Future: The Nanotechnology Revolution*, where the terms "nanobots" and "assemblers" were proposed for medical applications, and the concept of "nanomedicine" emerged [3].

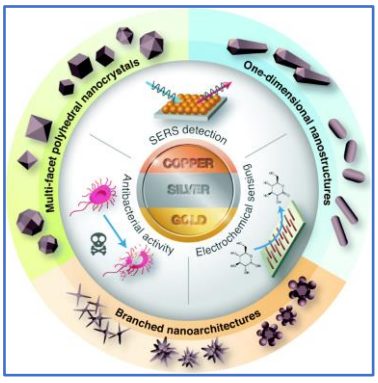

Fig. 1: General presentation of coinage metal nanostructures and their applications [4] (Reproduced with permission).

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Building on these concepts, many reports have highlighted the transformative potential of nanotechnology in biomedicine, including drug delivery systems, regenerative medicine, antibacterial nanoparticles, and nanoscale diagnostic devices such as bio-nanochips, nanoelectrodes, and biosensors. The prefix 'nano', derived from Greek meaning 'dwarf', refers to one-billionth of a meter (10^{-9} m). Nanotechnology deals with materials sized 1–100 nm, commonly termed nanoparticles. The general representation of coinage metal nanostructures can be seen in Fig. 1. The demand for nanoparticle fabrication is rapidly increasing due to their wide-ranging applications in healthcare, cosmetics, pharmaceuticals, electronics, optics, environmental remediation, and space technology. Such rapid developments have opened new avenues for research, fostering innovation across multiple scientific disciplines [5]. The rapid development of technology has paralleled the emergence of new diseases. As bacterial resistance increases, pathogens are becoming more resilient, creating a pressing need for novel antimicrobial strategies. Metal nanoparticles, their oxides, and composites such as copper and titanium dioxide have been widely explored for antibacterial applications, alongside other metals like Ag, Au, Pt, and ZnO etc [6]. The graphical representation of metal NPs can be seen in Fig. 2. Simultaneously, urbanization and industrial growth have improved living standards but also led to environmental pollution, as industrial effluents release chemically hazardous materials harmful to terrestrial and marine life. A key property distinguishing nanoparticles from their bulk counterparts is their high surface-to-volume ratio, which enhances the reactivity of metal ions and their effectiveness against microbial strains, offering a promising avenue for next-generation antibiotics [7]. Nanoparticles can be synthesized via two fundamental approaches: bottom-up and top-down techniques. In the bottom-up approach, nanoparticles are assembled atom by atom through chemical or biological methods, whereas top-down approaches involve breaking down bulk materials into nanoscale particles using techniques such as grinding, ball milling, sputtering, or laser ablation [8].

Nanoparticles with controlled size and morphology can be synthesized using chemical, physical, and biological methods, allowing their properties to be precisely tuned. Among these approaches, green synthesis is considered the most promising due to its non-toxic, eco-friendly, and cost-effective nature. Green synthesis, a bottom-up technique, utilizes plant extracts, biological products, or biomass as reducing agents instead of hazardous chemicals [18]. In this review, we focus exclusively on the green synthesis of copper (Cu) and titanium dioxide (TiO_2) nanoparticles using plant extracts. Numerous studies have reported the synthesis, characterization, and applications of Cu and TiO_2 nanoparticles [13–16]. However, this is the first review to compile research on the green synthesis of Cu and TiO_2, NPs via plant extracts.

Among noble metals, copper has garnered significant attention due to its unique properties, including chemical and physical stability, high thermal and electrical conductivity, photocatalytic activity, antibacterial and antifungal properties, and anti-inflammatory potential. These features enable copper nanoparticles to be incorporated into composite fibers, cosmetic products, the food industry, and electronic components [17]. Copper nanoparticles have attracted considerable attention due to their extensive applications in medicine, ranging from wound dressings to antiseptic fabrics. They are also explored for cancer treatment [18].

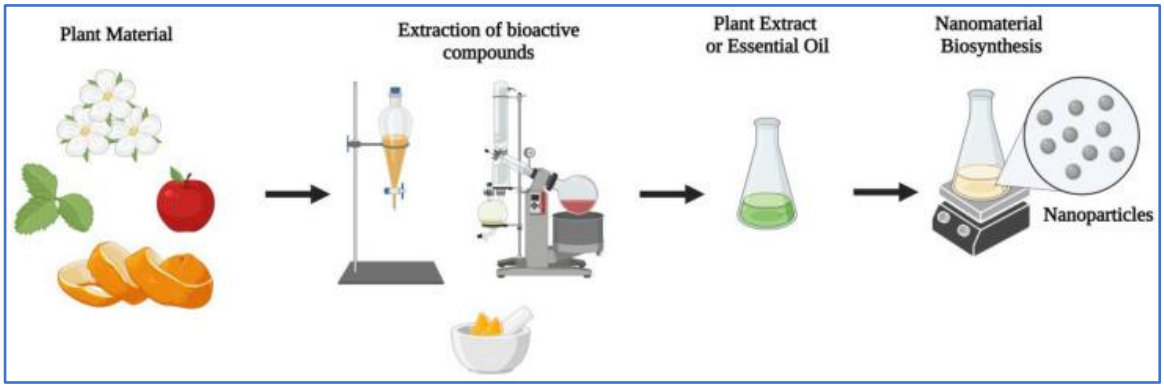

Fig. 2: Graphical representation of plant's leaves based green synthesis of metal NPs.

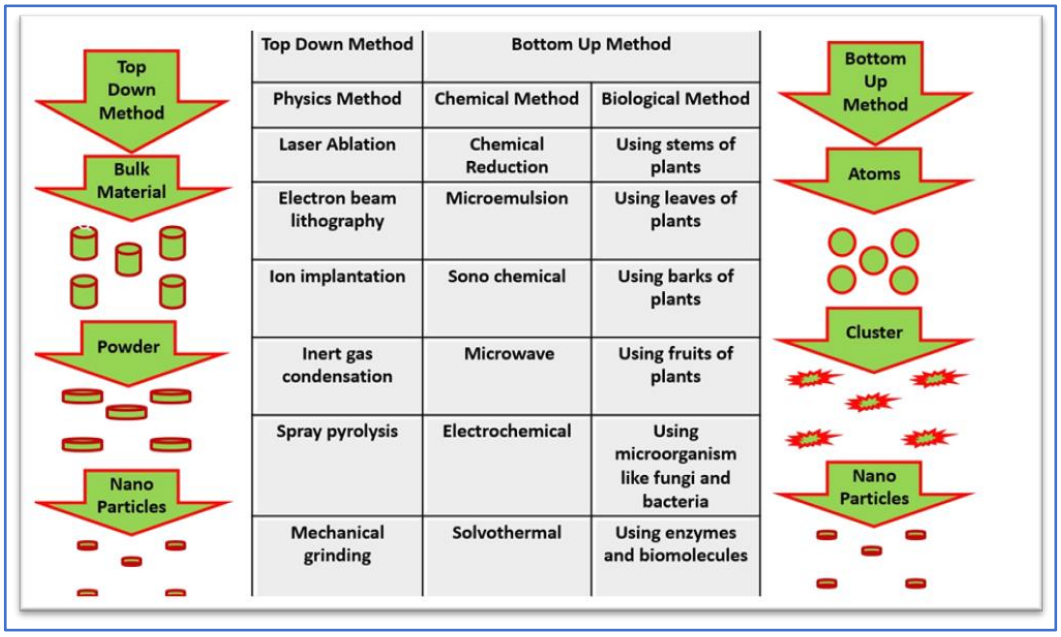

Fig. 3. Top-Down and Bottom-Up Approaches

Nanoparticles can be synthesized through two principal strategies. The top-down and bottom-up approaches. In the top-down method, bulk materials are progressively broken down into nanosized particles using physical or mechanical processes such as milling, lithography, or sputtering. Although this technique offers good control over particle size, it often results in structural defects and high energy consumption. Conversely, the bottom-up approach builds nanoparticles atom-by-atom or molecule-by-molecule through chemical or biological routes, including sol-gel, precipitation, and green synthesis using plant extracts. This method provides superior control over composition, shape, and crystallinity while being more cost-effective and environmentally friendly. In this review, emphasis is placed on the bottom-up green synthesis approach, which employs plant-derived phytochemicals as natural reducing and stabilizing agents to produce biocompatible and sustainable nanoparticles. Both of the approaches are detailed here in the Fig. 3.

TiO_2 NPs exhibit a wide range of applications, including photocatalysis, water treatment, self-cleaning materials, and energy storage devices [19–21]. TiO_2 has a large bandgap (~3.05 eV), enabling it to absorb ultraviolet radiation, a property widely exploited in cosmetics and skin care products. Its high refractive index makes it ideal for use as a white pigment. TiO_2 exists in three polymorphic forms: rutile, brookite, and anatase [22]. Rutile is the most common and thermodynamically stable form, while rutile and anatase have hexagonal crystal structures and brookite has an orthorhombic structure. The anatase form exhibits superior photocatalytic efficiency for degrading organic molecules [23]. TiO_2 also possesses antibacterial properties, which is a primary focus of this review. Researchers have worked to enhance its properties by controlling nanoparticle size and shape or by metal doping. Here, we specifically highlight Cu-doped TiO_2 nanoparticles for their enhanced antibacterial activity, combining the unique properties of both copper and TiO_2 for improved biomedical applications.

In this review, we first summarize plant-extract-mediated green synthesis routes for Cu and TiO_2 nanoparticles and highlight how key synthesis parameters influence particle size, morphology, and stability. We then outline the main characterization techniques used to evaluate optical, structural, and surface properties, noting common limitations and recommended practices. Next, we discuss the antimicrobial mechanisms of Cu- and TiO_2-based nanoparticles, including ion release, reactive oxygen species generation, and membrane disruption, followed by a focused overview of their antibacterial, antifungal, and antiviral performance. Finally, we review emerging biomedical applications such as anticancer activity, biosensing, and drug delivery, and conclude by discussing biosafety considerations and translational challenges.

To guide the reader, this review is well organized and structured in a efficient and stepwise manner. We first discuss plant-mediated green synthesis of Cu and TiO_2 NPs and summarize how synthesis variables and phytochemicals influence particle size, morphology, and stability. We then review major characterization techniques used to evaluate optical, structural, and surface properties, followed by an overview of antimicrobial mechanisms (ion release, ROS generation, and membrane disruption) and the reported antibacterial, antifungal, and antiviral performance.

Finally, we highlight key biomedical applications including anticancer activity, biosensing, and drug delivery and discuss toxicity, scale-up challenges, and future research directions.

Green Synthesis of Metal NPs

Green synthesis is an eco-friendly and sustainable process for synthesizing nanoparticles using natural resources and avoids harmful chemicals. This process utilizes microorganisms such as bacteria, fungi, yeast, and algae, or plant parts like leaves, roots, flowers, and fruits, as substrates [9]. Green synthesis aims to advance innovative chemical technologies that reduce or eliminate the use and production of hazardous substances in the design, manufacture, and use of chemical products. This approach focusing on minimizing or, if possible, eradicating the pollution produced in the synthesis processes, avoiding the consumption and wastage of nonrenewable raw materials, and reducing the use of hazardous or polluting materials in product manufacturing Additionally, it seeks to shorten synthesis times. Paul J. Anastas, known as the father of green chemistry, described it as "a work philosophy that involves using alternative tools and pathways to prevent pollution," encompassing both the design of synthetic strategies and the treatment of any secondary products that may arise [10]. The detailed presentation of metal NPs through green synthesis is detailed in the Fig. 4. [11].

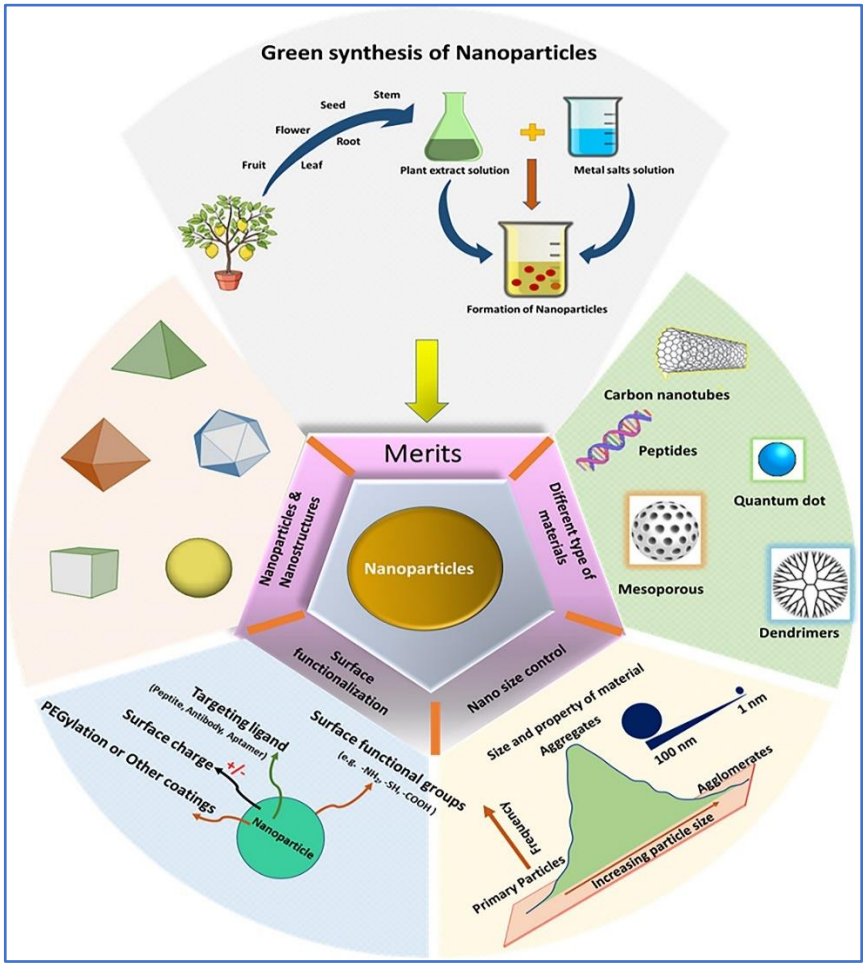

Fig. 4: Green Synthesis of Metal NPs [11].

The four phases for the green synthesis of nanoparticles include the initial phase, which firstly starts by obtaining an aqueous extract of one or several parts of the plant species or the culture media for the growth of microorganisms as the reaction medium, in addition to the precursor salt, which is the source of metal ions. The next stage is the activated stage, which involves the chemical reduction of metal ions and the formation of nucleation centers, where nanoparticles begin to form and develop. During the growth phase, nearby small nanoparticles spontaneously merge into larger particles, forming aggregates. This process is affected by factors such as temperature, concentration, types of compounds, pH, and the duration of the reaction. Finally, the nanoparticles achieve their ultimate shape in the termination phase and the compounds involved in the reaction assist in stabilizing and enhancing the properties of the nanoparticles, as shown in Fig. 5.

Green synthesis of Cu NPs using plant extracts

The single-step approach for green synthesis of copper nanoparticles has gained attention because of the non-toxic, eco-friendly and low-cost approach. The reduction and stabilization of copper nanoparticles with the help of biomolecules like alkaloids, phenolic compounds, Phytochemicals, and saponins present in plant extract is useful for the fabrication of nanoparticles. Several reports have been produced on the fabrication of copper nanoparticles. Copper nanoparticles and their synthesis approach are detailed in the (Fig. 6) given below. The prescribed details of nanoparticle fabrication involved the complete process from the collection of plants to the collection of nanoparticles. The selected leaves of plants are washed thrice with tap water to remove dust particles and later dried in the shade to avoid moisture. The healthy and undamaged leaves are washed with distilled water to remove the bio component. The leaves are ground and soaked in the de-ionized water to get leave extract. According to hot percolation method, approximately 10 grams of leaves are immersed in 100 ml of de-ionized water [12].

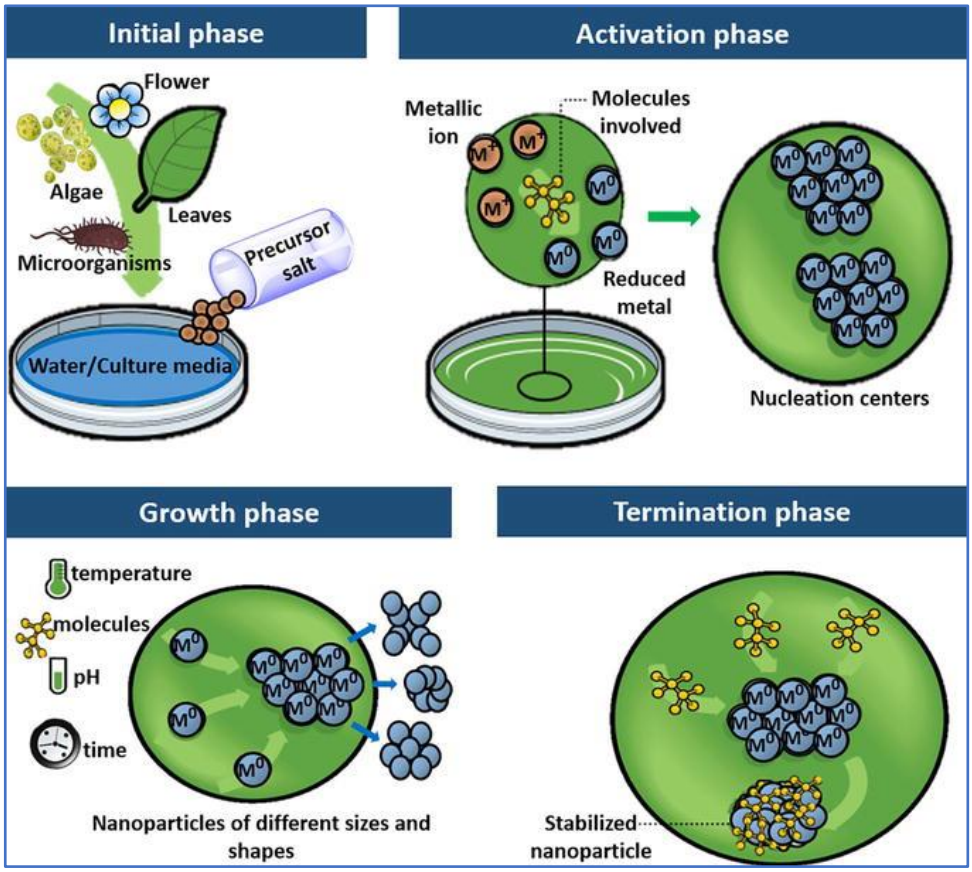

Fig. 5: Phases analysis of NPs synthesis.

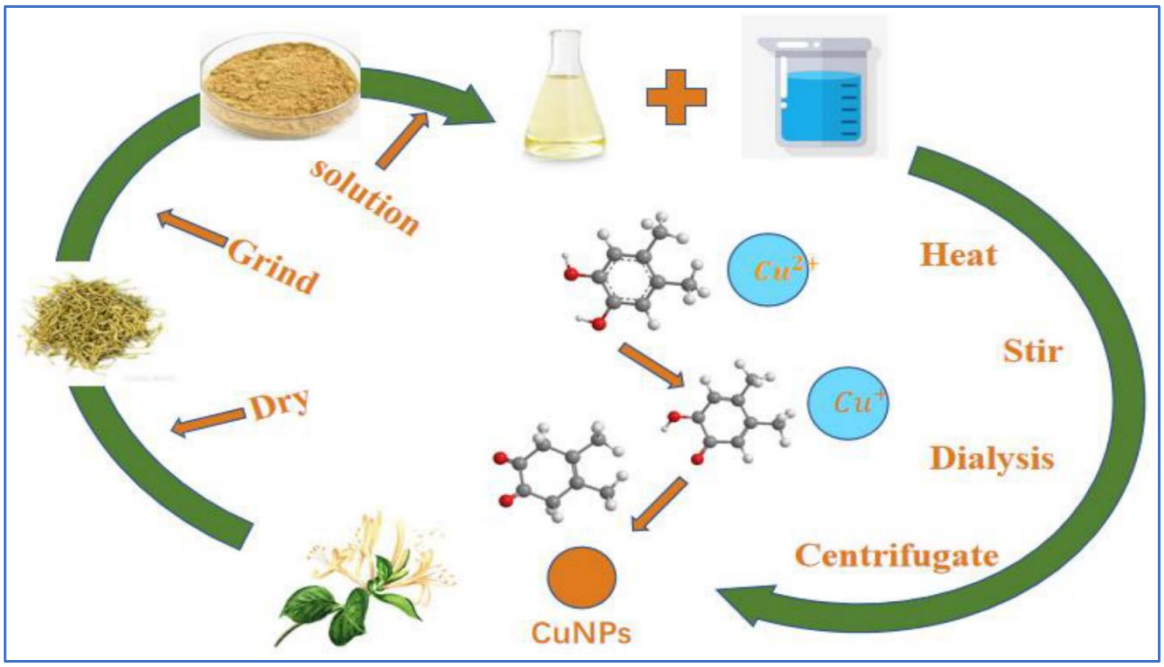

Fig. 6: Synthesis of Cu-NPs by green method [13].

The detailed literature survey of greenly synthesized Cu NPs is listed here in the Table. 1 where the size, shape, precursor and morphology of NPs is discussed in detail. Nazar et al. reported that *Punica granatum* seed extract reduced $CuCl_2$ to form spherical Cu nanoparticles (Cu NPs) of ~43.9 nm [14], while Singh et al., synthesized smaller (10–15 nm) spherical Cu NPs using *Asparagus adscendens* leaves [15]. Chung et al., obtained uniform 31 nm spherical Cu NPs from *Eclipta prostrata [16]*, and Narasaiah et al., achieved ~18.7 nm particles using *Drypetes sepiaria* extract [17]. Similarly, Alavi and Karimi produced ultrasmall (~4.8 nm) Cu NPs from *Artemisia haussknechtii* leaves [18], whereas Asghar et al., used black-tea extract to generate 26–40 nm spherical NPs [19]. Similar outcomes were observed with *Terminalia catappa*, *Aloe vera*, *Olea europaea*, and *Moringa oleifera* extracts [20-27]. Across these studies, spherical morphologies predominated, attributed to the stabilizing role of plant-derived polyphenols and flavonoids. Nanoparticle size and shape were found to strongly influence antimicrobial efficacy, as smaller Cu nanoparticles demonstrated increased reactive oxygen species (ROS) generation and improved bactericidal performance, highlighting the relevance of plant-mediated green synthesis for biomedical applications.

Table-1: Green synthesis of Cu NPs and their precursors for comparison of size and shape.

Sr No	Plants	Part of Plant	Precursor	Shape	Size	Citation
1	*Punica grantum*	Seeds	$CuCl_2$	Spherical	43.9 nm	[14]
2	*Asparagus adscendensroxb.*	Leaves	$CuSO_4$	Spherical	10-15 nm	[15]
3	*Eclipta prostrata*	Leaves	$Cu(CH_3COO)_2$	Spherical	31±1.2 nm	[16]
4	*Drypetes sepiaria*	Leaves	$(Cu(NO_3)_2.3H_2O)$	Spherical	18.7 nm	[17]
5	*Artemisia haussknechtii l*	Leaves	$CuSO_4$	Spherical	4.8 nm	[18]
6	*Black tea*	Leaves	$CuSO_4$	Spherical	26-40 nm	[19]
7	*Moringa oleifera*	Leaves	$CuSO_4.5H_2O$	Spherical	6-61 nm	[27]
8	*Aloe vera*	Leaves	$CuSO_4$	Spherical	15-30 nm	[22]
9	*Malus domestica*	Leaves	$CuSO_4$	Spherical	18-20 nm	[25]
10	*Terminalia catappa*	Leaves	$CuSO_4.5H_2O$	Spherical	21-30 nm	[21]
11	*Jatropha curcas*	Leaves	$CuCl_2$	Spherical	10 ± 1 nm	[28]
12	*Oak hull*	Fruit	$Cu(CH_3COO)_2$	Quasi Spherical	34 nm	[23]
13	*Olea europaea*	Leaves	$CuSO_4$	Spherical	20-50 nm	[24]
14	*Solanum lycopersicum*	Leaves	$CuSO_4.5H_2O$	Spherical	20-40 nm	[26]
15	*Cedrus Deodara*	Leaves	$CuSO_4.5H_20$	Spherical	-	[29]
16	*Plantago asiatica*	Leaves	$CuCl_2$	Spherical	7-35 nm	[30]
17	*Bauhinia tomentosa*	Leaves	$CuSO_4$	Spherical	22-40 nm	[31]

Although plant-mediated routes consistently enable Cu and TiO_2 nanoparticle formation, the reported size, morphology, and colloidal stability vary widely across plant species and even across studies using the same plant. This variability largely reflects differences in phytochemical profiles (e.g., polyphenols, flavonoids, terpenoids, alkaloids, sugars, and proteins) that act as both reducing and capping agents. Extracts rich in phenolics/flavonoids typically promote rapid nucleation and stronger surface passivation, which can favour smaller particles and improved dispersion stability, whereas lower capping density or weaker adsorption can allow growth and aggregation, yielding broader size distributions. In addition, extraction solvent and temperature influence the abundance of active metabolites, while synthesis parameters such as precursor concentration, pH, reaction temperature, mixing rate, and reaction time govern nucleation–growth kinetics and therefore final particle size and shape. These trends help explain why seemingly similar protocols can produce different nanoparticle outcomes and underline the need to interpret antimicrobial performance alongside size, surface chemistry, and aggregation state rather than particle diameter alone.

Despite its advantages, plant-mediated synthesis faces practical challenges related to reproducibility and scale-up. A major limitation is batch-to-batch variability in plant extracts caused by species differences, plant age, seasonality, geography, storage conditions, and extraction protocol, which can alter reducing strength and capping efficiency and lead to inconsistent nanoparticle size and surface chemistry. Reproducibility is further affected by incomplete reporting of key parameters (extract-to-precursor ratio, pH, temperature profile, stirring speed, and purification steps), making cross-study comparison difficult. For scalability, controlling heat and mass transfer, maintaining uniform mixing, and ensuring consistent phytochemical composition become more challenging as reaction volumes increase; downstream steps such as centrifugation, washing, and calcination can also become cost- and time-intensive at larger scales. Accordingly, future progress should emphasize protocol standardization and quality control, including basic extract characterization (e.g., total phenolic/flavonoid content), defined synthesis windows, and reporting of yield, stability (zeta potential/aggregation), and storage behaviour to enable reliable translation beyond laboratory scale.

Green synthesis of TiO_2 NPs using Plant Extracts

Extracts from different parts of the plant, e.g., stem, bark, root, flowers, seeds, etc. can be collected depending upon the plant used. Generally, the plant extract is collected from the selected part of the plant through different steps: washing, crushing, and boiling in a suitable solvent for a specific time. Later on, the solution can easily be filtered and used for the next process. Excessive heating may damage phytochemicals present in the plants. Soaking the plant for a longer time can help with better chemical extraction [32, 33]. Alcohol and phenolic solvents show more phytochemical content instead of deionized water but the selection of solvent may vary from plant to plant [33]. Usually, the synthesis of titanium dioxide nanoparticles is carried out with the addition of de- ionized water or ethanol solvent with the precursor of titanium. The most commonly used precursors of titanium are titanium tetra isopropoxide, titanium tetrachloride, metatitanic acid and titanium oxysulphate [34]. Bulk form of titanium is also used for the synthesis of titanium dioxide nanoparticles. The green extract is added dropwise into the precursor at a moderate temperature with constant stirring, the change in colour from brick to dark brick colour is the sign and the prediction of the formation of nanoparticles. The solution is centrifuged or filtered to get the solute. Different organic components from the solute are removed by calcination from 400 °C to 800 °C to get pure titanium dioxide nanoparticles [35]. The size of nanoparticles is controlled and stabilized using capping agents. Recently, there has been growing interest in green synthesis methods employing plant extracts, as the phytochemicals naturally act as both reducing and capping agents to stabilize nanoparticles. The schematic diagram is presented in Fig. 7. This approach also offers the advantage of producing nanoparticles on a large scale in a shorter time [36]. The details of part of the plant, precursor and shape of metal NPs is listed in the Table. 2.

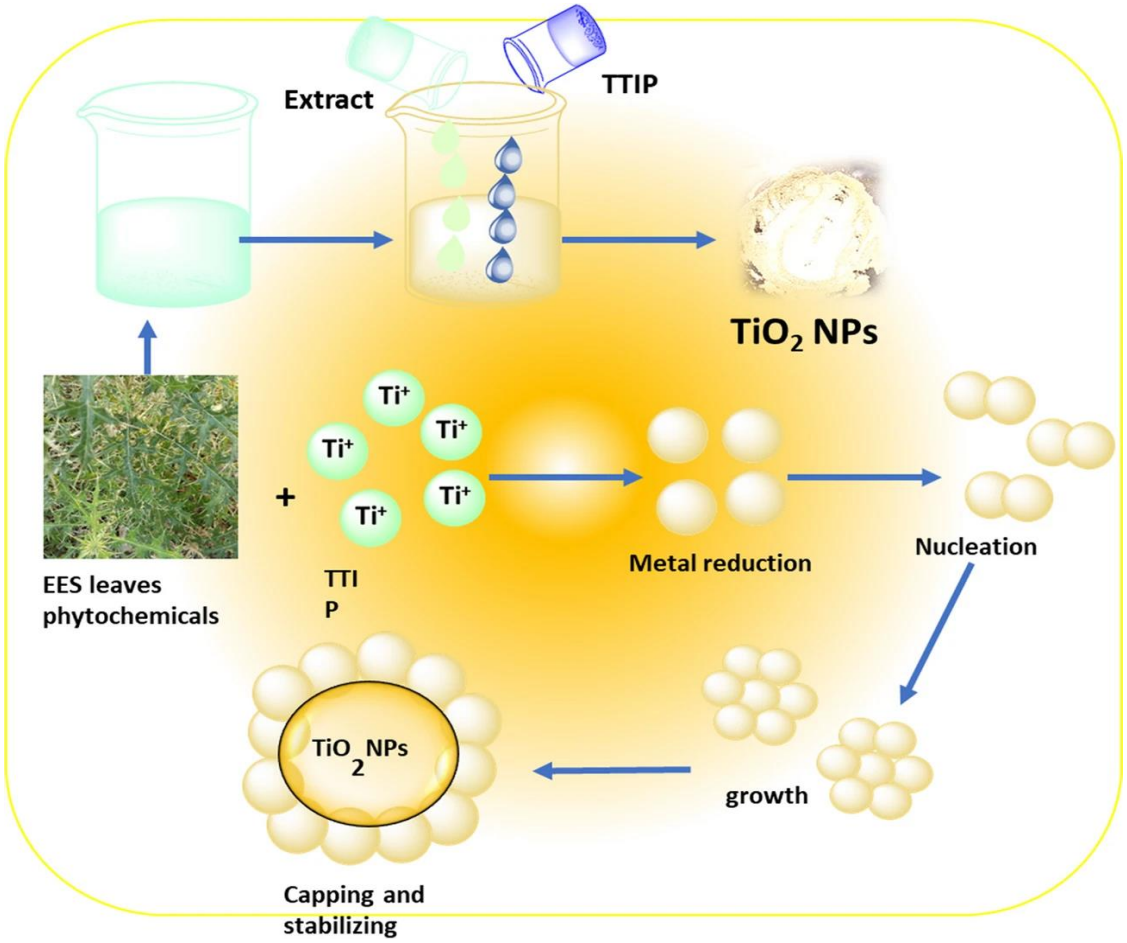

Fig. 7: Green synthesis of TiO_2 NPs via extract and plausible mechanism [36].

Table-2: Green synthesis of TiO_2 NPs.

Sr. No	Plants	Part of Plant	Precursor	Shape	Size	Citation
1	*Annona squamosa L.*	Peel	$TiO(OH)_2$	Poly disperse	23 nm	[37]
2	*Aloe vera*	Leaves	$TiCl_4$	Irregular	60 nm	[38]
3	*S. auriculata*	Leaves	$TiO(OH)_2$	Spherical	38 nm	[39]
4	*C. arietinum*	Seeds	$TiCl_4$	Spherical	14 nm	[40]
5	*Curcuma longa*	Powder	TiO_2	-	50 nm	[41]
6	*Dandelion*	Pollen	$TiCl_4$	Rod	50 nm	[42]
7	*E. prostrate*	Leaves	$TiO(OH)_2$	Spherical	36-68 nm	[43]
8	*E. prostrate*	Leaves	TiO(OH)2	Poly disperse	83.22 nm	[44]
9	*H. rosa sinensis*	Flower	TiSO2	Spherical	7-24 nm	[45]
10	*J. curcas*	Latex	TiO(OH)2	Spherical	25-100 nm	[46]
11	*Mangifera indica*	Leaves	$TiO(OH)_2$	Monodisperse	30±5 nm	[47]
12	*M. citrifolia*	Leaves	TiCl4	Spherical	15-19 nm	[48]
13	*Moringa oleifera*	Leaves	TiO_2	Spherical	100 nm	[49]
15	*O. basilicum*	Leaves	TiO_2	Hexagonal	50 nm	[50]
16	*P. betle*	Leaves	$Ti(OBu)_4$	Spherical	7 nm	[51]
17	*P. guajava*	Leaves	$TiO(OH)_2$	Spherical	32.58 nm	[52]
18	*V. radiate*	Legume	TiO_2	Oval	24 nm	[53]
19	*T. foenum graecum*	Leaves	$TiOSO_4$	Spherical	20-90 nm	[54]
20	*C. gigantea*	Flower	$TiO(OH)_2$	Spherical	10 nm	[55]
21	*Catharanthus*	Leaves	TiO_2	Cluster	25 nm	[56]
23	*Momordica charantia*	Leaves	$TiCl_4$	Poly disperse	34.6-70.4 nm	[57]
24	*P. hysterophorus*	Leaves	TiO_4	Spherical	20-50 nm	[58]
25	*Glycosmis cochinchinensis*	Leaves	$TiO(OH)_2$	Spherica	40 ±5 nm	[59]

Morphological Controlling and Characterization of NPs

It is reported that various extraction factors, including the method, time, temperature and solvent, greatly affect the nanoparticles' morphology and hence antioxidant property of plant-derived products [60, 61]. The ageing of crystals comprises all structural changes that occur in crystals after nucleation and crystal growth have occurred. Several different phenomena fall under the general classification of ageing. The ageing of the crystal shows the broad size of titanium dioxide nanoparticles and poor crystallinity, which can be improved by calcination. Heat treatment is applied to induce crystal growth. The large surface-to-volume ratio of nanoparticles as compared to bulk material is the key point for marvelous properties of nanoparticles for different applications [62, 63].

Characterization of the synthesized nanoparticles was carried out using various techniques. These included UV–Vis spectroscopy for determining optical properties and bandgap, Fourier transform infrared spectroscopy (FTIR) for identifying functional groups and chemical bonds on the nanoparticle surface, X-ray fluorescence spectroscopy (XRF) for measuring chemical composition, and X-ray diffraction (XRD) for evaluating crystallinity and grain size. The morphology and size of nanoparticles were examined using scanning electron microscopy (SEM) and field-emission scanning electron microscopy (FE-SEM), while elemental composition and concentration were analyzed by energy-dispersive spectroscopy (EDS/EDX). Finally, transmission electron microscopy (TEM) provided high-resolution imaging of nanoparticle morphology, size, and internal structure as shown in Fig. 8.

Challenges, Limitations, and Best Practices in Nanoparticle Characterization

Accurate characterization of plant-mediated Cu and TiO_2 nanoparticles is essential for correlating synthesis conditions with physicochemical properties and biological performance. However, several analytical limitations and practical challenges can lead to misinterpretation if not carefully addressed.

UV–visible (UV–Vis) spectroscopy is commonly employed as a rapid, preliminary tool to confirm nanoparticle formation through surface plasmon resonance or absorption edge features. While useful for monitoring reaction progress, UV–Vis analysis provides only indirect information and is sensitive to particle aggregation, solvent effects, and concentration, making it unreliable for precise size determination or phase identification. Fourier transform infrared (FTIR) spectroscopy is widely used to identify phytochemicals involved in nanoparticle reduction and capping. Nevertheless, overlapping vibrational bands from complex plant metabolites often complicate peak assignment, and changes in peak intensity alone cannot unambiguously confirm chemical binding to nanoparticle surfaces. FTIR results should therefore be interpreted cautiously and ideally supported by complementary surface-sensitive techniques. Electron microscopy techniques offer more direct structural insight but also present limitations. Scanning electron microscopy (SEM) provides information on surface morphology and agglomeration but may overestimate particle size due to limited resolution for nanoscale features. Transmission electron microscopy (TEM), in contrast, is the most reliable method for determining primary particle size, shape, and size distribution; however, sample preparation can induce aggregation or drying artifacts, potentially biasing measurements. Consequently, SEM and TEM results should be compared critically rather than used interchangeably.

X-ray diffraction (XRD) remains the most robust technique for assessing crystallinity and phase purity of Cu and TiO_2 nanoparticles. Crystallite sizes estimated using the Scherrer equation reflect coherent domain sizes rather than actual particle diameters and should not be directly equated with TEM-measured sizes. Combining XRD with electron microscopy enables more accurate structural interpretation. For surface chemistry and colloidal stability, zeta potential analysis provides valuable insight into dispersion behaviour and long-term stability in aqueous media, while energy-dispersive X-ray spectroscopy (EDX) confirms elemental composition but lacks sensitivity to surface-bound organic species. No single technique is sufficient to fully characterize green-synthesized nanoparticles; instead, a multi-technique approach is essential.

Best practices in nanoparticle characterization therefore, include: (i) combining optical, structural, and surface analyses rather than relying on a single method; (ii) clearly distinguishing between crystallite size and particle size; (iii) reporting sample preparation conditions; and (iv) correlating physicochemical data with antimicrobial or biomedical performance. Adopting these practices improves data reliability, cross-study comparability, and the translational relevance of plant-mediated nanoparticle synthesis.

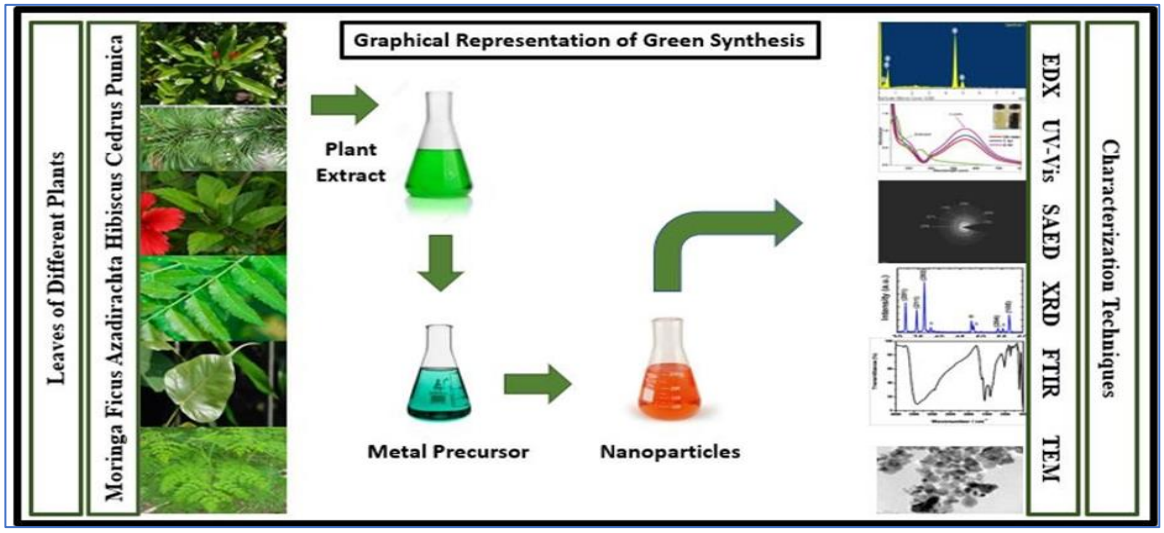

Fig. 8: The Characterization Techniques of Metal NPs.

Mechanism of Antimaterial Activity

The discovery of antibiotics in the twentieth century marked a turning point in modern medicine, ushering in what is often referred to as the *"golden era of antibiotics."* Since then, remarkable progress has been made in combating bacterial infections, with antibiotics becoming one of the most successful milestones in chemotherapy [64]. However, the continuous misuse and overuse of conventional antibiotics have led to the alarming rise of bacterial drug resistance, severely hindering the development of new, effective treatments [65]. Moreover, sessile bacterial communities are capable of forming biofilms, which enhance their defence mechanisms and promote multidrug resistance (MDR), posing a serious threat to global health [66]. The World Health Organization (WHO) recognizes MDR as one of the most pressing challenges of our time, estimating around 700,000 deaths each year caused by resistant infections a figure projected to soar to nearly 10 million annually by 2050 if no effective interventions are made [67]. This escalating crisis not only endangers human health but also carries profound social and economic consequences. Nevertheless, the past decade has seen no USFDA approval of new antibiotics targeting these 'superbugs,' [68]. The visualization can be seen as depicted in Figure 9 [11]

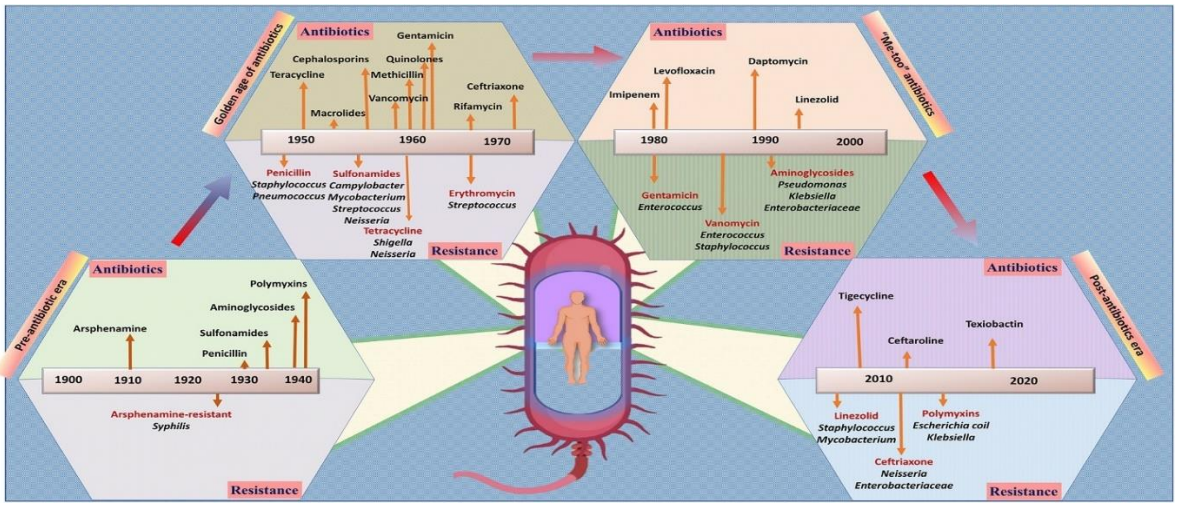

Fig. 9: Timeline of discovery of antibiotics and development of multi-drug-resistant bacteria [11].

Copper-based nanoparticles (metallic Cu, Cu_2O, CuO) release Cu^+ and Cu^{2+} ions at the NPS medium interface. These released ions bind electrostatically to negatively charged bacterial cell walls and fungal membranes, displace essential metal cofactors in enzymes, and interact with thiol (–SH) and amino groups in proteins [69]. Such interactions alter enzyme conformation, disrupt electron transport chains, and collapse membrane potential, ultimately increasing membrane permeability and causing leakage of cellular contents [70]. The rate of ion release and subsequent antimicrobial potency depend strongly on the oxidation state and surface chemistry Cu, Cu_2O, and CuO each exhibit distinct redox behaviours and ion dissolution rates [71]. The schematic illustration for the synthesis of Cu NPs is shown in Fig. 10 [72].

TiO_2 NPs, though chemically more stable and less soluble, can still release trace Ti^{4+} ions under physiological or acidic conditions. More importantly, TiO_2 surfaces interact with biomolecules through electrostatic adsorption and coordinate bonding, especially with phosphate, carboxyl, and amine groups on microbial cell walls or viral envelopes [73]. These interactions disturb membrane integrity, promote oxidative stress, and may facilitate penetration of nanoparticles into the cytoplasmic matrix. When illuminated (UV or visible light, depending on doping), TiO_2 further accelerates surface reactions that generate reactive oxygen intermediates and enhance ion exchange processes, amplifying its antimicrobial impact [74]. In recent years, TiO_2 nanoparticles have emerged as potent alternatives against antibiotic-resistant pathogens. Overuse of antibiotics has led to multidrug-resistant (MDR) bacterial strains, posing threats to food safety and human health. The antimicrobial efficiency of TiO_2 depends on microbial surface characteristics, the susceptibility order generally being viruses has more than bacterial walls and as more than bacterial spores. The schematic of antibacterial activity can be seen in Fig. 11 [75]. The photocatalytic generation of hydroxyl radicals induces oxidative stress on bacterial membranes, resulting in lipid peroxidation and disruption of essential processes such as respiration, oxidative phosphorylation, and membrane semi-permeability [76].

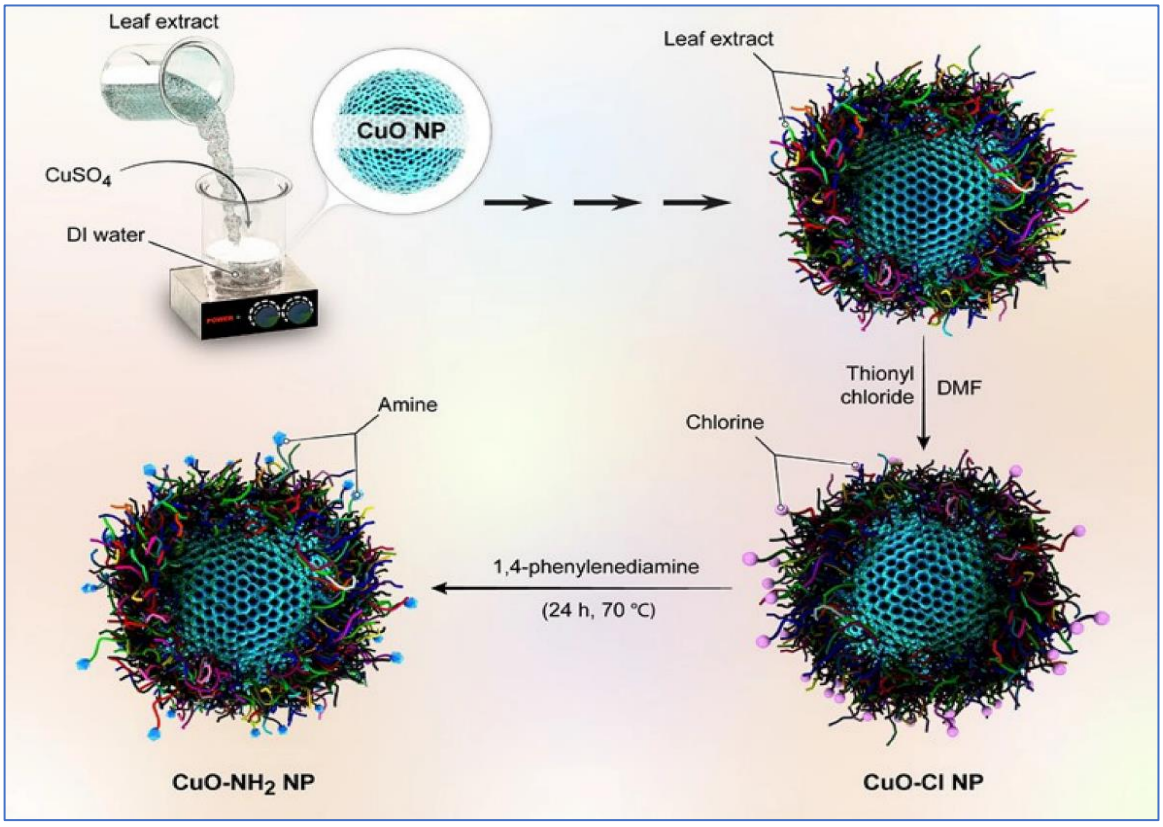

Fig. 10: The schematic illustration for the synthesis of CuO NPs [72].

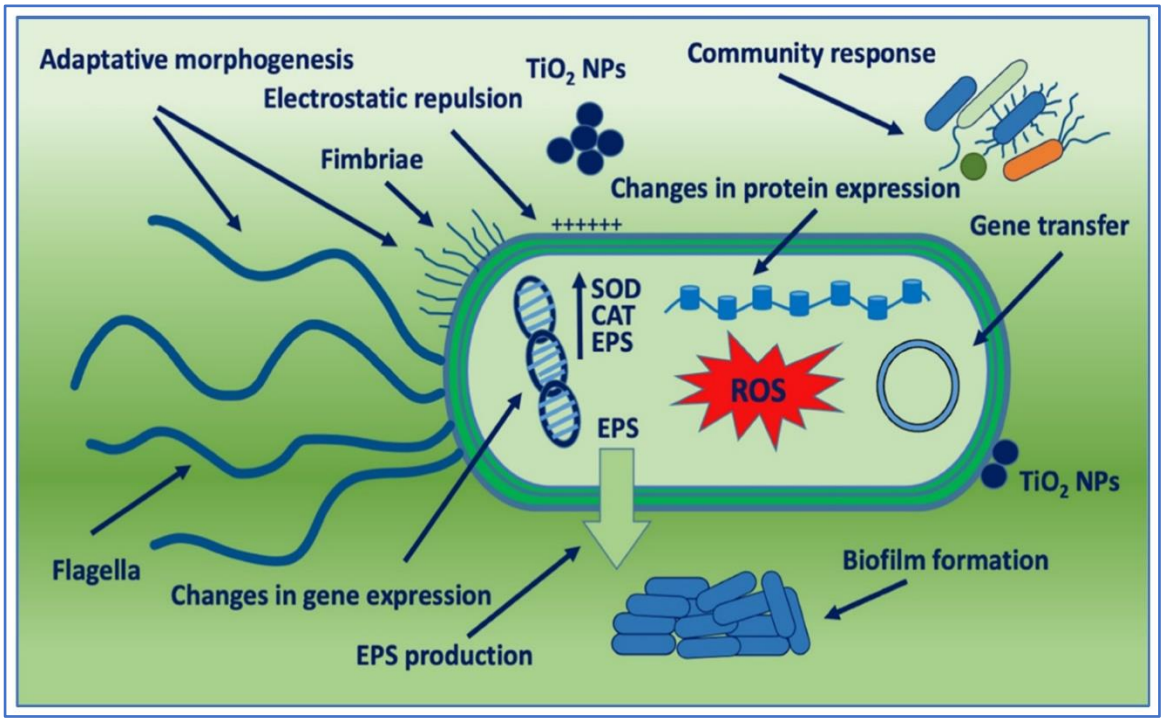

Fig. 11: The schematic representation of bacterial adaptation mechanisms against TiO_2 NPs [75].

Antimicrobial Potential Cu@TiO₂ NPs

Antibacterial Activity of Cu@TiO₂ NPs

Cu NPs and CuO show broad-spectrum activity against Gram-positive and Gram-negative bacteria. Efficacy depends on cell-envelope architecture: Gram-negatives' outer membrane (LPS layer) can confer extra resistance, but sufficiently small or ion-releasing NPs overcome this barrier [77]. TiO_2 is effective, especially when photo-catalytically activated (UV/visible) and can kill multidrug-resistant strains via ROS. Gram-positive and Gram-negative bacteria differ structurally: Gram-positives have thick peptidoglycan layers without an outer membrane, while Gram-negatives have an additional outer membrane that often impedes penetration of antibacterials. Thus, the mode of action of Cu (and TiO_2 to a degree) is influenced by these differences [78]. For example, Cu-incorporated TiO_2 surfaces, especially when designed with micro flower morphologies, have been shown in 2025 to produce complete inhibition against *Escherichia coli* (a Gram-negative) and *Staphylococcus aureus* (a Gram-positive) via Cu^{2+} ion release plus morphological effects [79]. Similarly, biosynthesized TiO_2 NPs reduced biofilm formation by ~94% against multidrug-resistant *Pseudomonas aeruginosa* (Gram-negative) isolates, and showed synergism with antibiotics [80]. Bacterial cells growing in biofilms: a matrix of polysaccharides, proteins, and nucleic acids is particularly hard to eliminate; here Cu NPs and CuO (and TiO_2 when activated) reduce biofilm biomass, metabolic activity, and viability. Recent work with $Cu_2Ti_2O_5$ nanoparticles reported ~86–89% biofilm formation reduction for *Klebsiella pneumoniae* and *P. aeruginosa* (Gram-negative) at 2×MIC and MIC, respectively, demonstrating that hybrid Cu/Ti materials also mediate strong antibiofilm effects under relevant clinical isolates. The schematic diagram of Gram-positive and Gram-negative bacteria can be seen here in Fig. 12 [81].

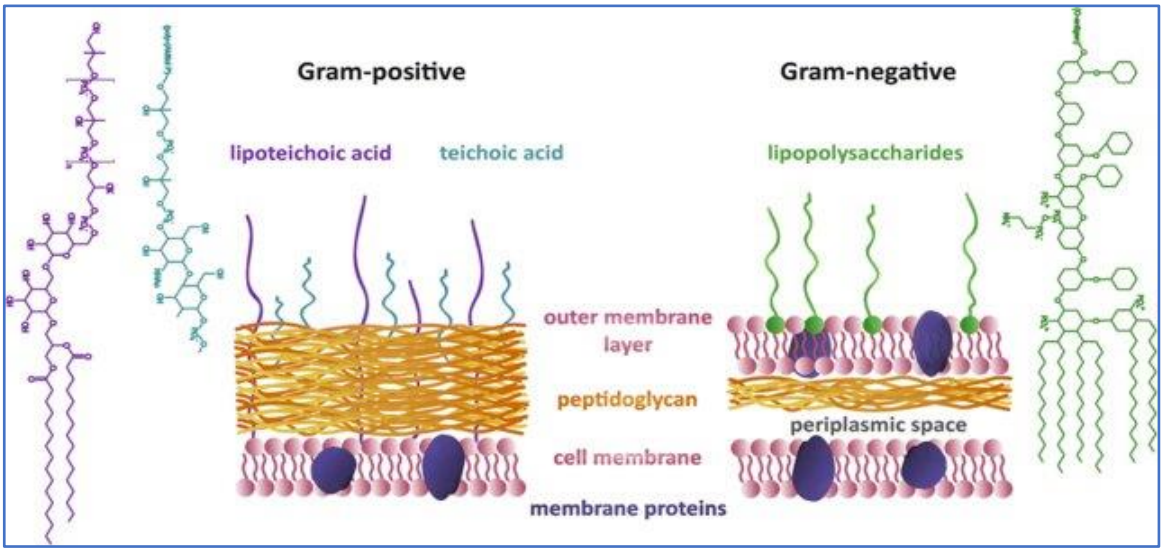

Fig. 12: The differences between Gram-positive and Gram-negative bacterial cell walls [81].

Table-3: Presents the antibacterial potential of Cu NPs.

Plant	Bacteria	Method	Citation
Gloriosa Superba L	*S. aureus*	Well diffusion	[82]
Syzygium aromaticum	*Bacillus spp.*	Disc diffusion	[83]
Aloe vera	*A. hydrophilia, P. fluorescens and F. Brachyphyllum*	Agar well diffusion	[84]
Stachys lavandulifolia	*Pseudomonas aeruginosa*	Agar well diffusion	[85]
Asparagus	*P. aeruginosa, E. coli, B. subtilis and*	Agar well diffusion	[15]
Tilia	*P. aeruginosa, E. coli, B. subtilis and S. aureus*	Well diffusion	[86]
Malus domestica	*E. coli and S. aureus*	Agar well diffusion	[25]
Olea europaea	*E. coli and S. aureus*	Disc diffusion	[87]
Guava	*E. coli and S. aureus*	Disc diffusion	[88]
Syzygium Cumin	*E. coli and S. aureus*	Well diffusion	[89]
Punica grantum	*M. luteus, P. aeruginosa, E. aerogenes*	Agar well diffusion	[90]
Nerium oleander	*E. coli, S. aureus, K. pneumoniae, S. typhi and B. subtilis*	Agar well diffusion	[91]
Vitis vinifera	*E. Coli and B. subtilis*	Agar well diffusion	[92]
Tabernaemontana divaricate	*E. Coli*	Well diffusion	[93]
Dodonaea viscosa	*E. coli, K. pneumonia, P. fluorescents, S. aureus, and B.subtilis*	Well diffusion	[94]
Camellia sinensis	*E. coli and Cereus*	broth inoculation	[95]
Glycosmis cochinchinensis	*E. coli, P. aeruginosa, S. saprophyticus and B. subtilis*	Kirby Bauer disc diffusion	[96]
Azadirachta indica	*E. coli, B. subtilis, S. typhi and K. Pneumonia*	Well diffusion	[97]
Cassia fistula	*S. aureus and E. coli*	Agar well diffusion	[98]
Cynodon Dactylon	*E. coli*	Agar well diffusion	[99]
Prunus yedoensis	*S. aureus and E. coli bacteria*	Agar well diffusion	[100]

Antifungal Activity of Cu@TiO_2 NPs

Both organic and inorganic nanoparticles with antifungal (antimycotic) properties have been developed, each offering distinct advantages and facing specific limitations. In this review, we primarily focus on inorganic nanoparticles, as they exhibit greater chemical and thermal stability than their organic counterparts. This enhanced stability allows them to be stored, transported, and applied more effectively, even under challenging environmental conditions [101]. We begin by discussing recent research on antifungal inorganic nanoparticles, including metal-based (silver, gold, and copper), metal oxide (zinc oxide, titanium dioxide, iron oxide, and copper oxide), transition-metal dichalcogenide (molybdenum disulfide and molybdenum diselenide), and inorganic non-metallic (carbon, selenium, and tellurium) nanoparticle systems [102-109]. Fungal cells possess robust cell walls composed of chitin, glucans, and glycoproteins, and are enveloped by membranes containing ergosterol [110]. Cu NPs release Cu^{+}/Cu^{2+} ions that interact with thiol and amino groups of proteins, destabilizing enzymes and collapsing membrane potential. TiO_2 NPs, particularly under UV or visible-light photocatalysis, generate hydroxyl radicals and superoxide ions, leading to lipid peroxidation, membrane damage, and disruption of vital metabolic processes. The vast scope of antifungal activity for Metal, Metal Oxide, TMDC NPs is shown in Fig. 13 [111].

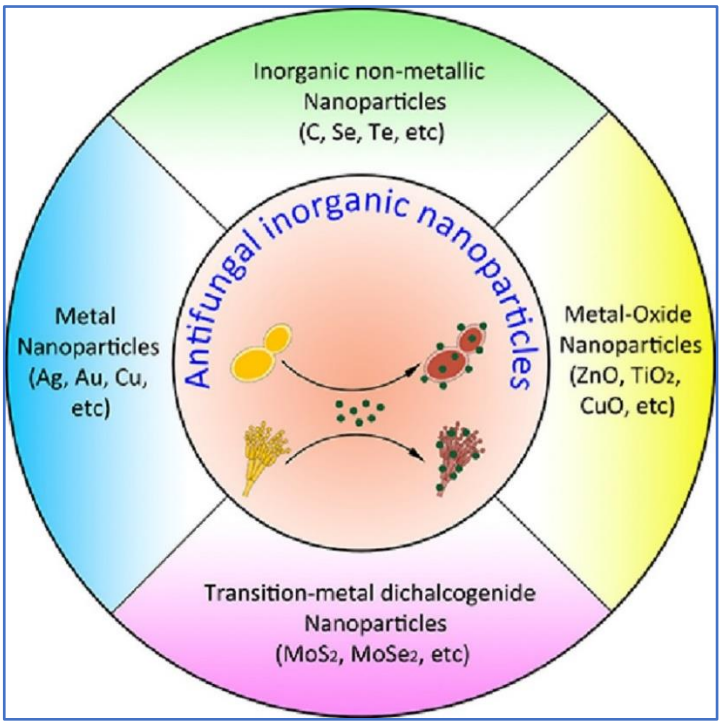

Fig. 13: The vast scope of antifungal activity for Metal, Metal Oxide, TMDC NPs [111].

Over the past few decades, the occurrence of invasive fungal infections has risen considerably. Each year, fungal infections affect over one billion people worldwide and are responsible for approximately 1.6 million deaths [112]. The majority of these fatalities around 90% are linked to four main fungal genera: *Candida* spp., *Aspergillus* spp., *Pneumocystis* spp., and *Cryptococcus* spp. [113]. Among them, infections caused by *Candida* spp. and *Aspergillus* spp. are particularly concerning, with mortality rates ranging between 30% and 50% [114]. *Candida* spp. alone account for nearly 40% of all deaths attributed to fungal infections [115]. In addition to invasive infections, superficial fungal diseases are also common, often involving species such as *Trichophyton* spp., *Epidermophyton* spp., and *Microsporum* spp. [116]. Consequently, managing and controlling fungal infections remains a critical public health priority. The growing problem of antimicrobial resistance further complicates this issue, as many opportunistic fungi have naturally developed resistance to several classes of antifungal agents [117]. The number of published reports have demonstrated a variety of different mechanisms by which inorganic nanoparticles exert their antifungal effects, including release of mycotoxic ions [118], damage to the membrane [119], protein [120], DNA [121], and other critical cellular components, ROS overproduction [122], and ATP depletion [123] as shown in Fig. 14. [124].

Collectively, these studies confirm that Cu and TiO_2 NPs, individually or in composite forms, disrupt fungal cell walls and membranes, generate ROS, and reduce spore viability, offering promising strategies against fungal infections. Hernandez et al., demonstrated that CuO/TiO_2 nanoparticles exhibit strong antifungal activity against *Candida albicans*, *Aspergillus niger*, and *Fusarium oxysporum* [125]. Similarly, Alabdallah et al., reported that TiO_2 nanoparticles effectively suppressed the growth of *Ustilago tritici*, the causal agent of wheat smut disease [126]. Garcia-Marin et al., presented that CuO nanoflakes show pronounced antifungal efficiency against *Candida albicans*, *Aspergillus flavus*, and *Fusarium oxysporum* [127]. Lastly, Damrongrungruang et al., revealed that TiO_2 nanoparticles combined with blue LED-mediated photodynamic therapy significantly disrupted *Candida albicans* biofilms, highlighting their promise in antifungal photodynamic applications [128]. The detailed fungal analysis of $Cu@TiO_2$ NPs is listed in Table. 4.

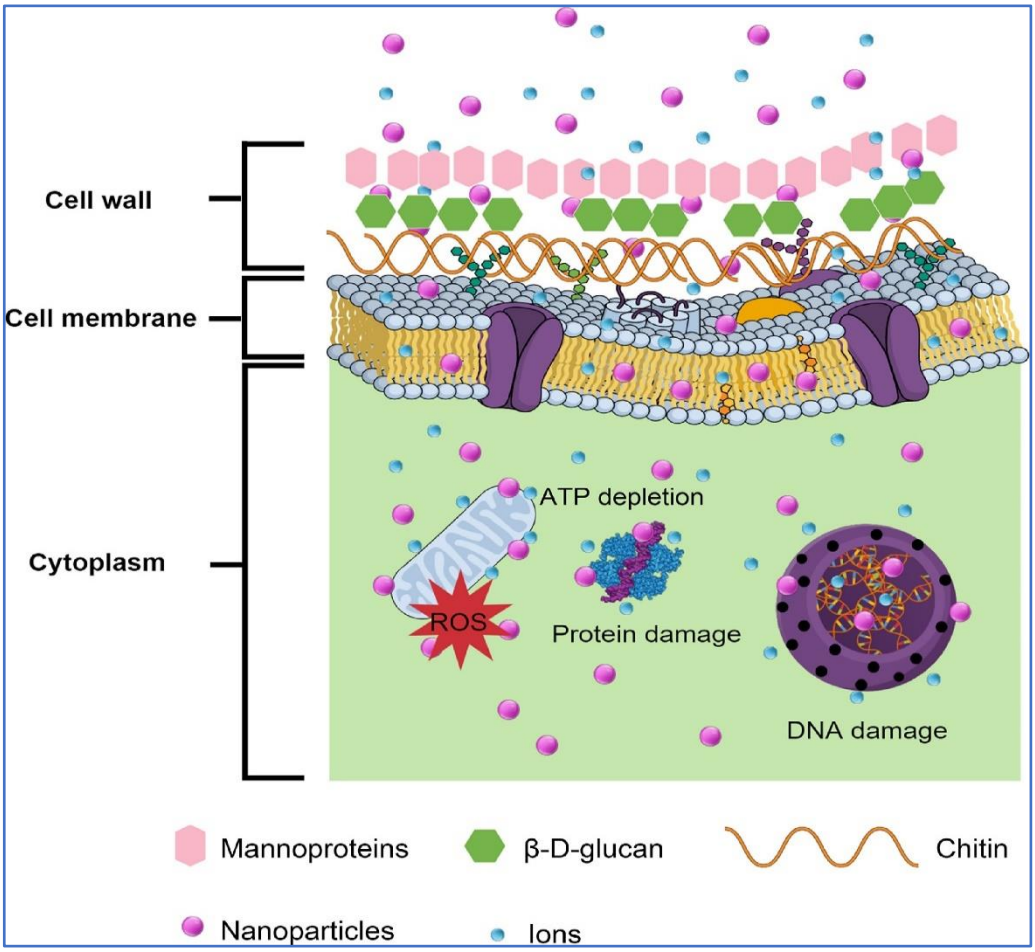

Fig. 14: Schematic showing some of the possible antifungal mechanisms of inorganic NPs. Inorganic NPs could adsorb on the surface of fungal cells and then enter the cell by transportation. Once inorganic NPs are in contact with the cytoplasm, they can affect the function of mitochondria and promote the production of ROS [124].

Table-4: Detailed analysis of Cu@TiO_2 NPs.

Nanoparticle	Target Fungi / Strain	Reference
CuO/TiO_2 NPs	*Candida albicans*, *Aspergillus niger*, *Fusarium oxysporum*	[129]
TiO_2 NPs	*Ustilago tritici*	[126]
TiO_2-Cu^{2+}/CuI Nanocomposites	*Candida parapsilosis*, *Aspergillus niger*	[125]
CuO Nanoflakes	*Candida albicans*, *Aspergillus flavus*, *Fusarium oxysporum*	[127]
CuO/TiO_2 NPs	*S. aureus and E. coli*	[130]
Ag/CuO	*Candida albicans*, *Aspergillus niger*, *Fusarium oxysporum*	[131]
TiO_2 NPs (Photodynamic Therapy)	*Candida albicans* (biofilm)	[128]

Antiviral Activity and Food Contamination

The COVID-19 pandemic has intensified awareness of viral contamination in food systems, driving interest in antiviral strategies for packaging. Embedding antiviral agents within packaging materials has emerged as an effective approach to inhibit viral survival and transmission. This review highlights recent progress in antiviral materials, including bioactive compounds, functional polymers, and inorganic nanomaterials, with emphasis on their mechanisms of viral inactivation and attachment prevention. Nanotechnology-enabled systems, such as nanocarriers and surface-modified films, are also discussed for their superior antiviral performance. Key considerations related to safety, regulation, and large-scale application are outlined to advance the development of antiviral active packaging which can be seen in Fig. 15 [132].

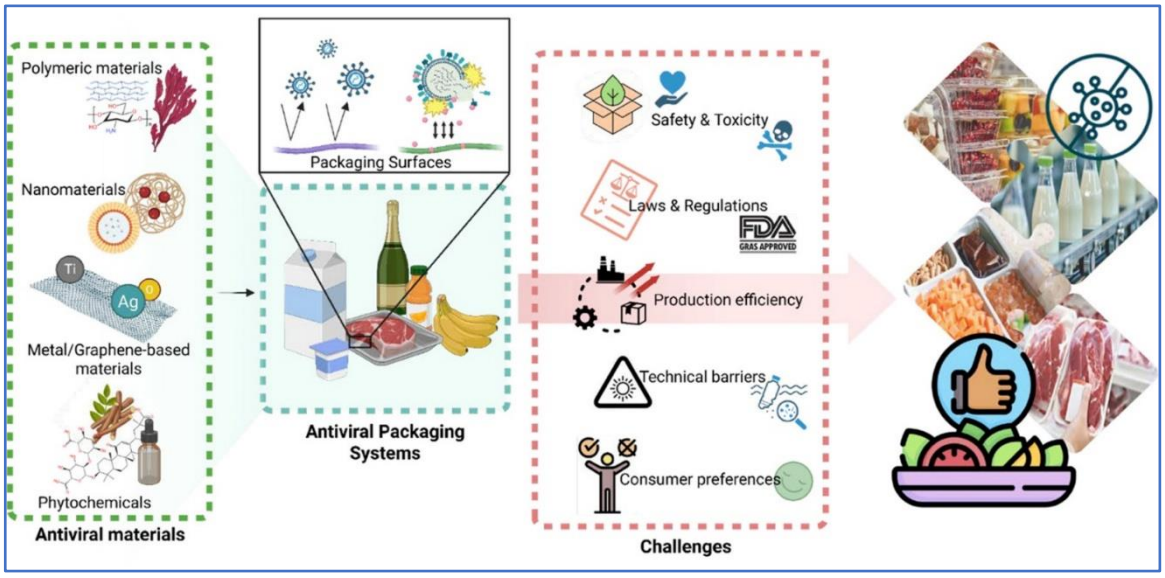

Fig. 15: Overview of antiviral food packaging strategies designed to prevent viral persistence and ensure food safety [132].

Food preservatives and antimicrobial packaging have long been used to prevent bacterial and fungal foodborne illnesses [133]. However, viruses also pose significant food safety risks. Norovirus alone causes an estimated 136,000–278,000 deaths annually, while hepatitis A outbreaks linked to contaminated food and water continue to occur worldwide [134]. T. Aftab et al., reported that in Pakistan, the Canal water, analyzed for physical, chemical, and metal parameters, showed that while most values met FAO standards, cadmium, copper, and chromium levels exceeded permissible limits, indicating contamination risks. [135]. Khan et al.., reported that the arsenic contamination in drinking water is a growing concern. Batch studies using low-cost adsorbents showed that microwave-activated date seed husk and lemon juice achieved the highest arsenic removal efficiency of 90%. [136]. Foodborne viruses, transmitted mainly via the faecal oral route, include norovirus, enterovirus, hepatovirus, rotavirus, astrovirus, and adenoviridae [137]. Moreover, evidence of respiratory viruses such as SARS-CoV-2 and influenza on food packaging surfaces highlights the need to broaden surveillance beyond traditional "foodborne" classifications. Table 1 summarizes key viral pathogens relevant to food safety. The type of virus, its family, sources and mechanism of action is detailed in the Table. 5.

Table-5: The type of virus, its family, sources and mechanism of action.

Virus	Family	Sources	Mechanism of infection	Refercens
Norovirus (NoV)	***Caliciviridae***	**Contaminated water, leafy vegetables, fresh fruits, bivalves**	**Binding to histo-blood group : unclear exact infection pathway**	**[138]**
Rotavirus, group A, B, C	***Reoviridae***	**Contaminated water, ice, fruit, vegetables,**	**Rotavirus outer capsid protein VP4**	**[139]**
Sapovirus (SaV)	***Caliciviridae***	**Contaminated water, raw or undercooked foods, bivalves**	**The cellular receptor for SaV entry remains unidentified**	**[140]**
Hepatitis A (HAV)	***Picornaviridae***	**Contaminated water, fruit, fruit juice, vegetables, milk or dairy products, raw**	**nHAV: Entry via binding to sialic acid-decorated proteins and lipids on hepatocytes;**	**[141]**
Nipah virus (NiV)	***Paramyxoviridae***	**Fruit bat of genus Pteropus as natural reservoir, fresh fruit and vegetables**	**NiV G protein mediates fusion via ephrin B2/B3 receptors**	**[142]**

Copper- and titanium dioxide-based NPs have demonstrated broad-spectrum antiviral activity against both enveloped and non-enveloped viruses through multiple physicochemical mechanisms. Cu nanoparticles and Cu-based nanostructures exhibit strong antiviral efficacy primarily via the release of Cu^{+}/Cu^{2+} ions, which interact with viral proteins and nucleic acids, leading to capsid destabilization, genome degradation, and inhibition of viral replication. In enveloped viruses, copper-mediated oxidative stress can damage lipid membranes and viral glycoproteins, thereby impairing host-cell attachment and entry. These mechanisms have been reported against viruses such as influenza, norovirus surrogates, and coronaviruses. TiO_2 NPs exhibit antiviral activity predominantly through photocatalytic generation of reactive oxygen species (ROS), including hydroxyl radicals and superoxide anions, which oxidatively damage viral capsid proteins, envelope structures, and RNA/DNA components. Even under low-light or modified surface conditions, TiO_2-based nanomaterials can reduce viral infectivity by disrupting surface proteins involved in host recognition. Surface-modified and doped TiO_2 NPs have shown enhanced antiviral performance, expanding their applicability under ambient conditions.

In the context of food-contact materials and environmental surfaces, incorporation of Cu and TiO_2 NPs into polymer matrices or surface coatings provides continuous antiviral functionality by limiting viral persistence and surface-mediated transmission. However, their antiviral efficacy is intrinsically linked to nanoparticle size, surface chemistry, dispersion stability, and exposure conditions, underscoring the importance of correlating synthesis parameters with antiviral performance.

Antimicrobial potential of Cu@TiO_2 NPs

Plant-mediated synthesis of copper and titanium dioxide nanoparticles provides an eco-friendly and sustainable route to produce antimicrobial nanomaterials with strong activity against Gram-positive and Gram-negative bacteria, as well as certain fungi and viruses. The increasing demand for safe, non-toxic, and sustainable nanomaterials has made green synthesis an appealing and widely adopted approach. Researchers across the globe have utilized diverse plant extracts for the fabrication of copper and titanium dioxide nanoparticles, highlighting their remarkable antimicrobial efficacy. Cu and TiO_2 NPs have emerged as highly effective antimicrobial agents due to their unique physicochemical properties at the nanoscale. Cu and CuO NPs release Cu^{2+} ions and generate ROS, which disrupt microbial membranes, proteins, and DNA, leading to rapid bacterial inactivation. For example, El-Kattan et al., reported that chitosan-capped CuO NPs (CS-CuO) achieved MIC values as low as 3.9–15.6 µg/mL against multi-drug-resistant clinical isolates, outperforming curcumin-capped CuO NPs (14.5–31.2 µg/mL) [143]. Similarly, plant-extract synthesized CuO NPs showed MICs of 62.5–125 µg/mL against multidrug-resistant bacteria. On the TiO_2 side, Cu_2O/TiO_2 composites demonstrated MIC = 16 µg/mL and MBC = 32 µg/mL under visible light against Pseudomonas marginalis, while surface-modified TiO_2 NPs with geraniol achieved MICs in the range 0.25–1.0 mg/mL and reduced MRSA biofilm thickness [144]. Hybrid CuO/TiO_2 nanomaterials applied on surfaces exhibited MICs of 0.312–0.625 mg/mL for S. aureus and E. coli, and functionalized lipase CuO conjugates further lowered MICs against multiple bacterial strains [145]. Collectively, these studies reveal that Cu and TiO_2 nanoparticles, especially when capped, surface-modified, or composited, possess potent antimicrobial properties, highlighting their potential in medical devices, coatings, water purification, and other applications where microbial contamination is a concern. The schematic and generalized concept of non-photocatalytic antibacterial actions of TiO_2 NPs is shown in Fig. 16 [146].

Biomedical applications of Cu@TiO_2 NPs

Anticancer therapy often involves the use of targeted treatments to destroy cancer cells while minimizing damage to healthy tissue. Nanoparticles are increasingly recognized for their advantages in cancer treatment. While chemotherapy remains a common approach, radiation and surgery have limitations, primarily due to the lack of targeted drug delivery. Nanoparticles offer a promising solution by providing more precise targeting of cancer cells, potentially improving the effectiveness of treatments and reducing side effects. Green nanotechnology aims to create eco-friendly nanoparticles for such therapies, leveraging plant-based methods to synthesize effective and less toxic treatment options. The in-vitro anticancer research works concluded that CuO NPs triggered intracellular ROS generation in a dose-dependent manner, significantly reducing cervical carcinoma colonies [147]. This promising outcome offers valuable insights for designing an improved anticancer compound using a plant-mediated synthesis of CuO NPs, aiming to minimize side effects. For example, the Acalypha indica leaves (NPs: spherical 29 nm) indicated the antibacterial and antifungal effect against Escherichia coli, Pseudomonas fluorescens and Candida albicans, and anti-cancer activity against MCF-7 human breast cancer cell-line [93, 148]. Antioxidants are essential in combating oxidative stress and protecting cells from damage. Green nanotechnology focuses on using sustainable methods, such as plant-based extracts, to produce nanoparticles that enhance the efficacy of antioxidants. This approach not only promotes health but also aligns with eco-friendly principles. Recently, one of the noteworthy research studies concluded that the leaf extract of Tribulus terrestris, a plant with high medicinal value, was effectively used to produce CuO NPs. This method proved to be lowcost, simple, and effective.

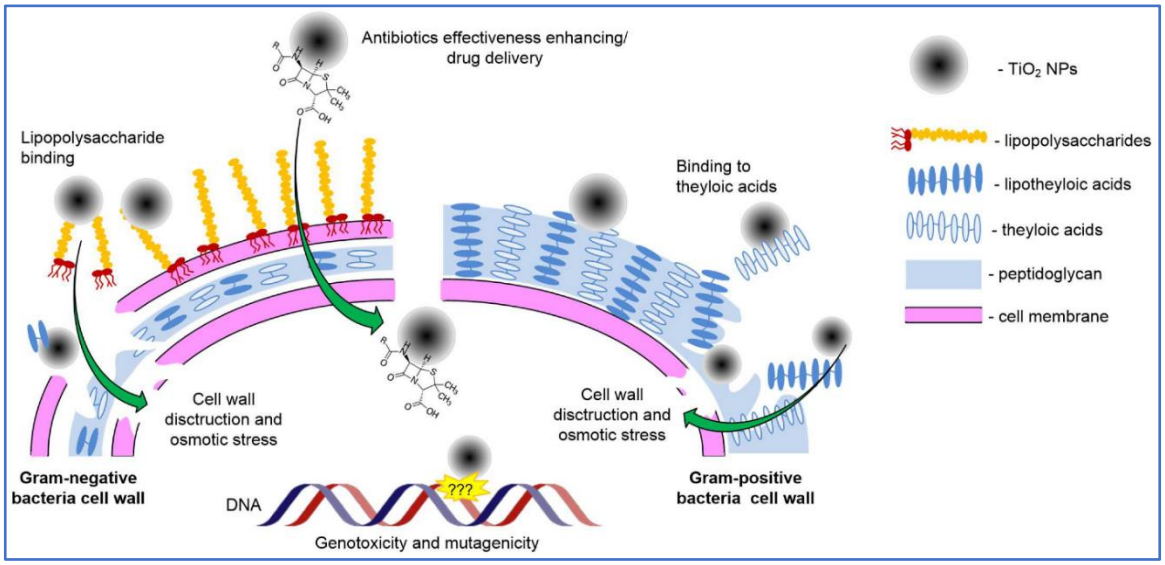

Fig. 16: The schematic diagram of non-photocatalytic antibacterial actions of TiO_2 NPs [146].

Nanotechnology has unlocked many new pathways, particularly in targeted drug delivery systems, thanks to metallic nanoparticles (MNPs) and their unique properties. Silver, gold, palladium, titanium, zinc, and copper nanoparticles, among others, are extensively used as carriers for various therapeutic agents such as antibodies, nucleic acids, chemotherapeutic drugs, and peptides. What makes MNPs particularly valuable are their enhanced, adjustable optical properties. Their surfaces can also be easily modified to attach targeting agents and active biomolecules through mechanisms like hydrogen bonding, covalent bonding, and electrostatic interactions. This flexibility allows for multiple drugs to be loaded simultaneously, leading to higher therapeutic effectiveness [149]. Copper nanoparticles possess specific capabilities for drug loading and effective photoluminescence, making them suitable for targeted delivery of anti-cancer drugs. The action of Cu nanoparticles can potentially degrade DNA by generating singlet oxygen. Additionally, these nanoparticles can induce cytotoxic effects on cancer cells through apoptotic induction. This suggests the potential for designing chemical modifications of Cu nanoparticles to create active molecules that interact with various macromolecules [150].

Timely detection of diseases can significantly boost the effectiveness of therapies by enabling rapid diagnosis and treatment. To enhance health management, biosensors, which employ biological recognition components to detect disease biomarkers, have been utilized. Recent advancements in biosensor technology have resulted in the creation of highly accurate, precise, robust, and swift systems that can detect disease-related changes in analyte levels. This capability allows for the prompt diagnosis and treatment of various diseases. Additionally, integrating biosensor platforms with drug delivery systems has yielded even more effective treatment strategies for biomedical applications, such as diabetes management [151]. Khaliq et al., developed a non-enzymatic cholesterol biosensor based on TiO_2 nanotubes decorated with Cu_2O nanoparticles, achieving improved accuracy and sensitivity in detecting cholesterol levels in blood [152]. Kumar and Sinha reported a glucose biosensor using Cu_2O nanoparticles deposited on TiO_2 nanotube arrays, enabling rapid and precise measurements of glucose concentrations in diabetic patients [153]. Carrapiço et al. highlighted the use of CuO nanoparticles in antibacterial biosensors, which can effectively detect bacterial contamination on medical equipment, enhancing sterilization and safety [154]. Ramyadevi et al. demonstrated that CuO nanoparticles could assess antioxidant activity in food products, providing a reliable means to ensure quality and safety [155]. Bertel et al., investigated TiO_2 nanostructured surfaces for environmental sensing applications, showing their effectiveness in detecting pollutants in water for monitoring and cleanup purposes [156]. Recent advances in nanotechnology have facilitated the development of innovative biosensors. Copper and titanium nanoparticles, particularly those synthesized via green methods, have demonstrated significant potential across diverse applications in biosensing, as illustrated in Fig. 17. [157]. The list of various sensors based on Cu and TiO_2 are listed in Table. 6.

Table-6: The name of sensor and functionlaity.

Sensor Name	Functionality	Citation
Non-enzymatic Cholesterol Biosensor	Detects cholesterol levels in blood using Cu_2O and TiO_2 hybrid nanostructure for improved accuracy and sensitivity	[152]
Glucose Biosensor	Measures glucose concentration in diabetic patients using Cu_2O nanoparticles on TiO_2 nanotubes for rapid and precise readings	[153]
Antibacterial Biosensor	Detects bacterial contamination in medical equipment using CuO nanoparticles for effective sterilization	[154]
Antioxidant Activity Sensor	Assesses antioxidant activity in food products using CuO nanoparticles to ensure quality and safety.	[155]
Eco-Contaminant Sensor	Detects pollutants in water using TiO_2 nanoparticles for environmental monitoring and cleanup.	[156]

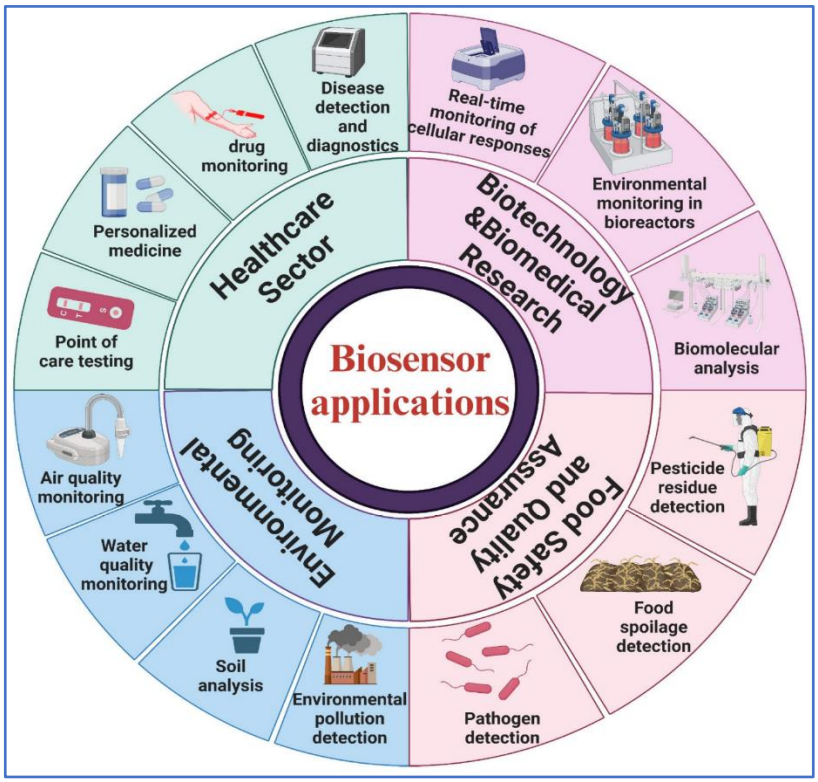

Fig. 17: Various uses of biosensors in healthcare, biotechnology, environmental monitoring, and food safety [157].

Cu@TiO₂ Nanoparticles: Mechanisms and Biomedical Potential

Copper-decorated titanium dioxide nanoparticles (Cu@TiO₂ NPs) combine the distinct antimicrobial mechanisms of both metals, offering synergistic antibacterial and antiviral activity. Cu ions released from the composite disrupt microbial membranes, displace essential metal cofactors in enzymes, and interfere with electron transport, while TiO_2 contributes through surface adsorption and photocatalytic generation of reactive oxygen species (ROS) under UV or visible light, leading to oxidative damage of microbial proteins and nucleic acids. This dual-action enhances efficacy against multidrug-resistant bacteria and a broad spectrum of viruses, as demonstrated by comparative MIC/MBC (bacteria) and IC50/EC50 (virus) data. Beyond in vitro studies, Cu@TiO₂ NPs show promise for biomedical applications such as antimicrobial coatings, wound dressings, and antiviral surfaces; however, careful evaluation of cytotoxicity, hemocompatibility, and in vivo biodistribution is essential. Light-dependent ROS generation and ion release kinetics must be optimized to maximize antimicrobial potency while minimizing toxicity, bridging the gap between laboratory-scale studies and potential clinical implementation.

Conclusion

This review highlights the first comprehensive effort to correlate the green synthesis mechanisms of copper and titanium dioxide nanoparticles using plant extracts with their physicochemical properties and antimicrobial activities. The study establishes that nature-derived

phytochemicals serve as effective reducing and capping agents, enabling the eco-friendly and cost-effective fabrication of stable, biocompatible nanoparticles. Unlike previous fragmented reports, this review uniquely combines insights on both Cu and TiO_2 nanostructures within a single framework, emphasizing their synergistic potential in combating multidrug-resistant pathogens and advancing biomedical applications. This review examines both Cu and TiO_2 nanoparticles and introduces a comparative green-synthesis framework relating phytochemical composition to nanoparticle stability and biological activity. These insights provide a new direction for future research, fostering the development of hybrid Cu@TiO_2 nanocomposites and other multifunctional systems for targeted drug delivery, biosensing, and antimicrobial applications for safer, sustainable, and high-performance nanomaterials in modern medicine.

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