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DERLEME MAKALESİ (Review Article)

THE SYNTHESIS OF NANOPARTICLES AND THE CURRENT APPLICATION IN DIFFERENT DOMAINS

Tugce AGACBOZAN[1], Ipek COBAS[2], Gulsade SAHIN[3], Dilay TASKIN[4], Nail OZSULUOGLU[5], Ferhat UZEN[6], Alattin BOLUT[7], Fatih SEN[8*]

[1] Sen Research Group, Department of Biochemistry, Dumlupinar University, Kutahya, Türkiye, tugceagacbozan123@gmail.com, ORCID: 0000 0001 8154 3274
[2] Sen Research Group, Department of Biochemistry, Dumlupinar University, Kutahya, Türkiye, ipek.cobas@ogr.dpu.edu.tr ORCID: 0000-0002-9259-3389 ,
[3] Sen Research Group, Department of Biochemistry, Dumlupinar University, Kutahya, Türkiye, gulsade.sahin@ogr.dpu.edu.tr ORCID: 0000-0003-2149-2158
[4] Sen Research Group, Department of Biochemistry, Dumlupinar University, Kutahya, Türkiye, dilaytaskin237@gmail.com, ORCID: 0000-0003-1411-276X
[5] Sen Research Group, Department of Biochemistry, Dumlupinar University, Kutahya, Türkiye, nail.ozsuluoglu@ogr.dpu.edu.tr, ORCID: 0000-0002-8787-7635
[6] Sen Research Group, Department of Biochemistry, Dumlupinar University, Kutahya, Türkiye, uzenferhat1@gmail.com ORCID: 0000-0001-9077-5026
[7] Sen Research Group, Department of Biochemistry, Dumlupinar University, Kutahya, Türkiye, alaattinbolut@gmail.com , ORCID: 0000-0002-3053-0286
[8] Sen Research Group, Department of Biochemistry, Dumlupinar University, Kutahya, Türkiye, fatihsen1980@gmail.com, ORCID: 0000-0001-6843-9026

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ABSTRACT

Nanomaterials are one of the most popular materials that can be used in many fields in recent years. According to the related definition, these materials are known to be formed by the combination of at least one size less than 100 nm or very small materials. In nanomaterials, size is very important as it generally provides information about their structure and properties. There are different synthesis methods for the production of nanomaterials. The most preferred method among these is the environmentally friendly green synthesis method. This method is a cost-effective, environmentally friendly, non-toxic biological method. addition, the usage areas of nanomaterials vary depending on their size. At this point, the dimensions of nanomaterials are; It can change their thermal, mechanical, optical, electrical, and magnetic properties. At the same time, nanomaterials are widely used in the materials and manufacturing industries, the medical-health industry, aerospace research, environmental and energy systems, biotechnology, agriculture, and food industries. In light of this information, within the scope of the study; The green synthesis production method of nanomaterials, their dimensions, general properties, and characterizations used to determine their physical and chemical properties are mentioned. In addition, research on drug release, antimicrobial, antifungal, anticarcinogenic, and environmental applications of nanomaterials were presented. Within the scope of these studies, it has been seen that nanomaterials are very interesting in the health sector, their applications should be increased, and it has been concluded that nanomaterials can produce solutions for many diseases with these applications. In addition, the data obtained show that nanomaterials with properties that can be used in many areas are very promising for the future.

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***Keywords**: Biotechnology, Nanomaterials, Nanotechnology, Green synthesis*.

NANOPARÇACIKLARIN SENTEZİ VE FARKLI ALANLARDA GÜNCEL UYGULAMALARI

ÖZ

Nanomalzemeler son yıllarda birçok alanda kullanılabilen en popüler malzemelerden biridir. Bu malzemelerin ilgili tanıma göre en az bir boyutu 100 nm'den küçük veya çok küçük malzemelerin bir araya gelmesiyle oluştuğu bilinmektedir. Nanomalzemelerde genellikle yapı ve özellikleri hakkında bilgi sağladığı için boyut çok önemlidir. Nanomalzemelerin üretimi için farklı sentez yöntemleri bulunmaktadır. Bunlar arasında en çok tercih edilen yöntem çevre dostu yeşil sentez yöntemidir. Bu yöntemin uygun maliyetli, çevre dostu, toksik olmayan biyolojik bir yöntem olduğu bilinmektedir. Ayrıca nanomalzemelerin kullanım alanları boyutlarına göre değişmektedir. Bu noktada nanomalzemelerin boyutları; Termal, mekanik, optik, elektriksel ve manyetik özelliklerini değiştirebilir. Aynı zamanda nanomalzemeler, malzeme ve imalat endüstrilerinde, medikal-sağlık endüstrisinde, havacılık araştırmalarında, çevre ve enerji sistemlerinde, biyoteknolojide, tarım ve gıda endüstrilerinde yaygın olarak kullanılmaktadır. Bu bilgiler ışığında çalışma kapsamında; Nanomalzemelerin yeşil sentez üretim yöntemi ve genel özellikleri, boyutları, ilaç salımı, antimikrobiyal, antifungal ve antikarsinojenik özellikleri ve çevresel uygulamalarına değinilmiştir. Elde edilen veriler doğrultusunda birçok alanda kullanılabilecek özelliklere sahip nanomalzemelerin gelecek için umut verici olduğu görülmektedir.

Anahtar Kelimeler: *Biyoteknoloji, Nanomalzemeler, Nanoteknoloji, Çevre dostu sentez*

1. INTRODUCTION

The origin of the term nanotechnology comes from the Greek word 'nano' meaning 'small'. Nanoparticles range in size from 1 to 100 nanometers and are very small particles. Nanotechnology: It is a science that examines biological, chemical, and physical structures and usage areas. Nanotechnology can be defined as essentially consisting of the separation, assembly, and deformation of materials by an atom or a molecule. Today, nanotechnology activities are widely used, especially in the fields of industry and medicine, and facilitate human life. The main features that make nanotechnology different from other branches are those materials behave more uniquely in this dimension than in the macro-Earth. The weight/power ratio, optics, conductivity, and magnetic properties change significantly as you move from the macro to the nanoscale. Developed countries such as the USA, England, Germany, Singapore, Japan, and Austria conduct and use detailed research on nanotechnology and size. At this point, nanotechnology has become a brand-new and groundbreaking science with all its features [1–4]. Size is very important in nanotechnology and the nanomaterials that come with it, and these materials are examined in 4 classes according to their dimensions (zero, single, two, three dimensional). Of these materials, zero-dimensional nanomaterials; is the name given to materials whose entire scale is at the nanoscale. They are different materials in the form of nanopowder or nanodispersion. Today, these materials exist in different structures and are produced by various research groups. For example, quantum dots, nanospheres, fullerenes, core nanoparticles, and hollow nanospheres. One-dimensional (1D) nanomaterials are materials that have two dimensions at the nanoscale and one dimension at the microscale. One-dimensional nanomaterials

can be polycrystalline or single-crystalline, while impure nanomaterials can be chemically pure. Some nanomaterials can be used on their own, but some may be embedded in the matrix. Examples of one-dimensional nanomaterials are carbon nanotubes and metal oxide nanotubes, one-dimensional nanomaterials. Two-dimensional (2D) nanomaterials are materials that are one-dimensional at the nanoscale and two-dimensional at the microscale. Today, two-dimensional nanomaterials have become more valuable and their usage areas are quite common compared to others [5]. Examples of two-dimensional nanomaterials are graphene, boron nitride, molybdenum disulfide, nanofilms, and nanocoating. Finally, three-dimensional (3D) nanomaterials are the name given to materials that do not have any dimensions at the nanoscale. The most important differences that distinguish three-dimensional nanomaterials from other types are distinctive differences such as high surface area [6], surface porosity, optical, electrical, and magnetic properties. Examples of three-dimensional nanomaterials are hydrogels and metal oxide lattices. When the application areas of these nanomaterials are examined, it is seen that they are widely used [6]. For example, In the food industry, nanomaterial applications are used to improve food packaging for quality and reliable food production and to ensure traceability of food using biosensors. At the energy point, it increases lighting and heating efficiency, increases electricity storage capacity, and reduces pollution in energy production used for cleaning. For this sector, for example, the importance of nanomaterials used for new generation batteries, fuel cells and super capacitors has increased today [7]. In addition to these, nanomaterials are also widely used in the field of health. At this point, it is seen that it is widely used in antibacterial, anticancer, carrier drug systems [8]. Nanomaterials are promising for many fields and today many studies are carried out on nanomaterials. [9,10]. At this point, it is important to increase the production and application areas of these materials.
Within the scope of the study, the production methods of nanomaterials with superior properties were mentioned in general and it was shown that they have different application areas. At this point, attention was drawn to the green synthesis method, one of the production methods, and especially drug delivery systems and antibacterial applications were emphasized. In addition, the effects of nanomaterials on the environment and human health are also discussed. By compiling these studies, general information is given about the development and important effects of nanomaterials, especially in the field of health.

2. NANOMATERIAL SYNTHESIS

Various synthesis methods are used to obtain nanomaterials. These synthesis methods can be said as 3 main topics, biological, physical, and chemical methods. Among the mentioned methods, the most environmentally friendly, simple, and easy method is the biological method. This method of synthesis is not limited to microorganisms but is also carried out using plant parts.

2.1. Physical Synthesis of Nanomaterials

This synthesis method is divided into two top-down and bottom-up. In the top-down synthesis method, coarse materials are turned into powder using the grinding technique. The disadvantage here is the difficulty of obtaining the desired particle size and shape [11]. When the particles obtained here are compared with normal particles, it is seen that there are deviations in the magnetic properties of the samples prepared with defects in the lattice parameters due to grinding synthesis [12]. In bottom-up synthesis methods, nanoparticles in the liquid and gas phases are condensed. In this process, large materials are obtained by combining small ions. Physical synthesis methods are detailed in the table below [13–19].

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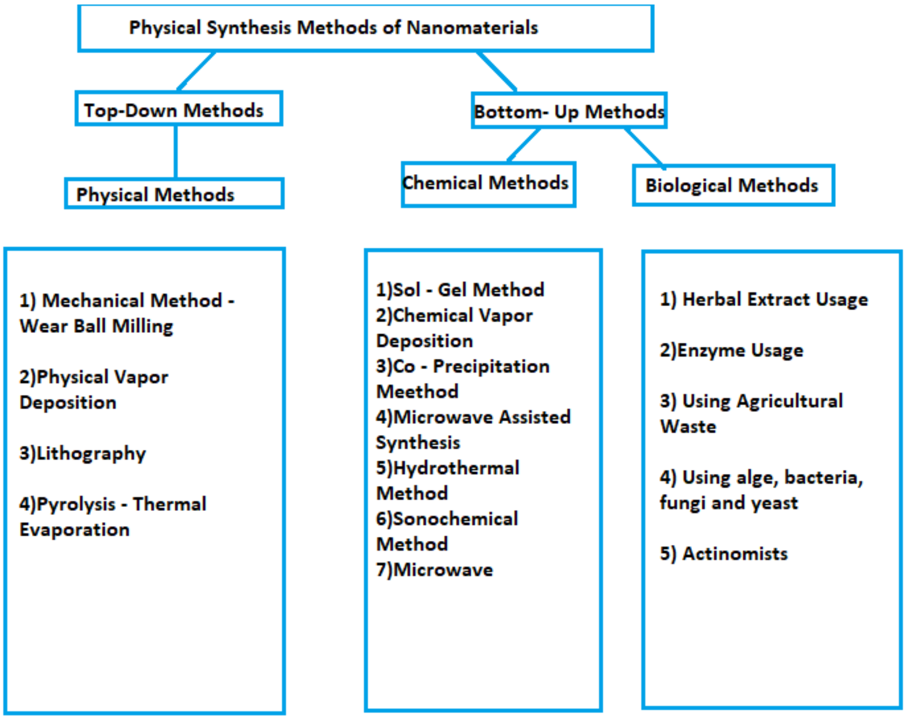

Figure 1. Synthesis methods of nanoparticles [13–19].

2.2. Green Synthesis of Nanomaterials

As mentioned above, there are two approaches in the synthesis methods of nanomaterials: top-down and bottom-up. In the first approach (top-down), large volumes of materials are broken into nano-sized pieces. The second approach (bottom-up) is the opposite of the first approach and uses single atoms to transform them into large materials. In addition, nanomaterial synthesis methods fall into two main categories. One of them is the traditional method and the other is the green method. The use of green synthesis is more common, as the potential harms of the traditional method outweigh the benefits. A clean, safe, and environmentally friendly process is used in the green synthesis method. In this method, microorganisms such as bacteria, yeast, fungi, and algae act as substrates. At this point, the benefits from green synthesis extend to antimicrobial, natural reducing, and stabilizing properties. In this synthesis, some of the green species are composed of specific enzymes, amino acid groups, proteins, or chemical structures [16,20–23].

2.2.1. Herb and herb extract

In the green synthesis method, plant and food residues are used to create, without exception, the most interesting and environmentally friendly nanomaterials. In this synthesis, certain chemical compounds must be removed from plants and food wasted. Plant and food wastes are dried, ground, or cut to remove these chemical compounds. After these processes are done, it is filtered and stored at 4C°[24]. These obtained reagents have a range of bioactive molecules depending on the specific plant and plant materials from which they are extracted. These plant extracts contain flavonoids, terpenoids, and phenols. [25,26] Plant extracts are not only limited to these compounds but also proteins, glycosides, and polysaccharides play a role in the synthesis of these nanoparticles[24,27,28]. In this synthesis method, a chemical that would be risky for the environment is not needed.[29] According to the literature, the most widely used nanoparticle type synthesized by plant material is silver nanoparticles.[30] The silver nanoparticle synthesis process is carried out with different plant materials for reducing, stabilizing, and capping substances in the extracts.[31,32] These are tea polyphenols, vegetable oil, capsicum corneum, hemp Sativa, and black currant. These herbs also act as reducing, stabilizing, and limiting agents as we have mentioned before. The most common plant material found in kitchens is vegetable oils. Another agent to be used in the synthesis of nanoparticles is aloe vera. Aloe vera is also used in traditional medicines and sunburns. As a result, the field and application of nanomaterials are expanding and continue to be researched. Conventional synthesis methods of nanomaterials (left-gel, chemical vapor deposition, laser ablation, pyrolysis, ultrasound, and hydrothermal) are harmful to the environment. Green synthesis methods cause little or no harm to the environment as previously stated. The chemicals used in the synthesis stage cause environmental damage. That’s why today, the use of green synthesis is emphasized.

2.2.2. **Synthesis of nanomaterials using microorganisms**

The most used microorganisms in studies using microorganisms are bacteria, algae, and fungi. These organisms contribute to the preparation of nanomaterials with an aqueous solution of metal salts. In the use of bacteria in biological synthesis, living organisms participate in the synthesis method using protein. For example, magnetotactic bacteria living on the seafloor and in anaerobic conditions use protein-coated magnetosomes to synthesize nano-sized magnetic iron oxide crystals and prepare the particles in the direction of their preferred habitat with a compass. [33,34]. In the use of fungi in biological synthesis, the fungus Fusarium oxysporum is used to synthesize extracellular nanoparticles. Today, studies on nanoparticle synthesis methods using algae are continuing. Algae extracts are easily synthesized and do not degrade rapidly. Algae are used as reductants in nanoparticle synthesis.

2.2.3. **Use of biological templates and synthesis of nanomaterials**

In this synthesis method, dissimilar and complex nanostructures are produced using protein and DNA. The main product used for nanocomposite materials is proteins. DNA templates are also used to assemble these particles.

3. CHARACTERIZATION OF NANOMATERIALS

Various techniques are used in the characterization process of nanomaterials. Thanks to these techniques, the structures of nanomaterials are better elucidated. The most commonly used techniques are X-ray diffraction (XRD), Transmissive electron microscopy (TEM), Atomic force microscopy (AFM), Scanning electron microscope (SEM), X-ray Photoelectron Spectroscopy (XPS), Raman Spectroscopy, Fourier transform infrared spectroscopy (FTIR). Apart from these techniques, Fluorescent correlation spectroscopy (FCS), Raman scattering (RS), Surface development Raman (SERS), Tip-enhanced Raman spectroscopy (TERS), Near field scanning optical microscopy (NSOM), Circular dichroism (CD), Mass spectroscopy (MS), Infrared spectroscopy (IR), Scanning tunneling microscope (STM), Nuclear magnetic resonance (NMR), Small angle x-ray scattering (SAXS) characterizations. Among these techniques, the most frequently used techniques are explained in detail.

3.1. XRD

This method is generally used in the examination of the internal structure of the substance with x-rays, in the determination of crystals, in the measurement of grain size, and in the qualitative and quantitative analysis of polycrystals[35,36]. The XRD technique is also used to characterize crystal size, shape, and lattice distortion in long-range order [37]. As a result of this technique applied to dusty samples, properties such as crystal structure as well as grain size are determined. Of course, this technique is used in liquid samples as well as powder samples. But with this technique, the best result is observed in powder samples. To measure the samples, the powder samples are placed in their special holders and placed in the special part of the XRD device, and the samples are analyzed. As the scope of XRD application; It is important in qualitative and quantitative analysis of samples of different thicknesses, geological samples, materials science and engineering, thin film analysis, cable industry, biomaterials, clinical samples, metal and alloy analysis, polymer analysis, archeology (detection of materials that make up historical buildings), ceramics and cement industry [38].

3.2. TEM

The principle of this device is based on the imaging of high-energy electrons passed through a very thin sample.[39] This device allows us to obtain direct images and chemical information of nanomaterials at a spatial resolution down to atomic dimensions. This device transmits the incoming electron beams over a very thin foil sample. Meanwhile, electrons interacting with the sample; are converted to unscattered electrons, elastically scattered electrons, or inelastically scattered electrons [40]. TEM has advantages over SEM. TEM is better than SEM for spatial resolution[39].

3.3. AFM

This device is a very versatile tool because it not only creates images on a 3D surface but also allows scientists and engineers to make various surface measurements according to their needs [41]. For this device to display an image, the needle at the end of the device must interact with the surface. In this way, the device can display images. The needle at the end of this device changes for different purposes and is examined using different tips. Here, besides only imaging the sample surfaces; phase is determined by electrical, conductivity, and magnetic differences. This technique is also a technique capable of imaging biomaterials without damaging the natural surface type and additional analytical measurements [42].

3.4. SEM

SEM is a surface imaging technique. At the same time, the size, size distribution, and shape of nanomaterials are obtained directly by this method [43]. The lenses in this device are used to control the characteristics of the beam sent to the device. Electrons interact with the sample from electron and photon signals. Conductive samples, coated insulation samples, powder samples, thin films, biological samples, and polymers can be examined in SEM [44].

3.5. FTIR

FT-IR spectroscopy is a frequently preferred technique in basic sciences, health sciences, and engineering fields, with the identification of bonds in the structure of molecules [45]. The basis of this technique is based on the absorption of movements such as vibration and rotation of the bonds of infrared rays falling on the intramolecular bonds. This method is also used for the determination of intramolecular bonds, the determination of the molecular formula, and the examination of functional groups[46]. This method is valid only for polar molecules with dipole moments. A molecule is capable of absorbing IR radiation if it has a time-varying dipole molecule and its oscillation frequency is the same as the frequency of the incident IR light. [47]. Diatomic molecules cannot absorb IR radiation. This method also includes matching pairs of atoms and covalent bonds. Therefore, the IR spectrum showing the absorption or absorption corresponding to the IR frequency can be presented as a fingerprint of the molecule of interest [48].

3.6. SERS

This device works by inelastic scattering of light falling on the bonds by intramolecular bonds [49]. This device is generally used in the fields of basic sciences, medicine, pharmacy, and engineering [50]. This device is also used to examine the melting mechanisms of volatiles such as H_2O, CO_2 and H_2 in aluminum cyclase melts and glasses. SERS also has ultra-high sensitivity and selectivity, and studies on SERS are promising in the future [51]. With SERS, it is possible to determine the chemical and structural information of the samples, determine homogeneity and purity, distinguish stem cells from differentiated cells, and analyze polymer mixtures.

3.7. XPS

SOFC, the surface of the cathode layers is a technique used to study elemental composition. This technique is also used to quantitatively analyze the surface electronic structure of the crystalline solid. The XPS device determines the kinetic energy of the electrons in the sample to be measured. İn this way, the device reveals the electron energy distribution in the material. This device not only provides information about the above-mentioned conditions. It also gives information about the binding energy of certain core levels, the chemical composition near the surface region, and the oxidation of an element [37].

4. APPLICATION OF NANOMATERIALS

4.1. The Role of Nanomaterials in Drug Delivery Systems

Nano-sized materials are used in life science, aerospace, medicine, electronics, and agriculture [52]. There are differences in mechanical properties between conventional materials and nano-sized materials. The mechanical properties of metals consist of ten parts. These are brittleness, strength, plasticity, hardness, toughness, fatigue strength, elasticity, ductility, rigidity, and yield stress. Inorganic non-metallic materials are also brittle. On the other hand, the mechanical properties of nanomaterials are more suitable due to volume, surface, and quantum effects. As nanomaterials are added to the base material, the particles are refined to a certain extent. In this case, it allows improvement in mechanical properties. For example, By adding nano-SiO_2 to the concrete, the compressive and tensile strength is increased [53].
Nanocarriers are used in gene delivery, targeted drug delivery, imaging, artificial implants, and biosensors. In short, it has many uses in medicine, from diagnosis to treatment [54,55]. The most common uses are in cancer treatments and drug delivery systems. In classical method drug applications, it should be applied in certain doses during the day. At the same time, these doses should not be given at low or toxic levels. In this case, drug delivery systems using nanocarriers come into play. Many types of nanomaterials are used in drug delivery systems, from nanoparticles to fullerenes [56,57]. The small structures of these nanomaterials provide significant advantages [58].

4.1.1. Nanoparticle

Nanoparticles can be synthesized by both natural and chemical methods. Therefore, it is the materials that attract attention. Today, natural synthesis methods are in demand. The best example of this method is green synthesis. Gold and silver nanoparticles synthesized by green synthesis are among the best metal nanoparticles in drug delivery systems [59,60] at the same time, it is environmentally friendly [61]. AgNPs have been the subject of research in the field of nanomedicine due to their high

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specific surface area, and special chemical, and physical properties [62]. Studies conducted, it has given positive results in every experiment in terms of multi-drug resistance, especially against chemotherapeutic agents [63]. At the same time, its known antibacterial properties have made AgNPs more useful. [59,64] Gold nanoparticles (AuNPs) are nanoparticles that attract attention with their optoelectronic and physicochemical properties [65]. With its ability to modify, it can enter application areas such as biosensors, diagnostics, DNA, and drug delivery [66,67]. AuNPs have a biosensing role. However, thanks to their large surface areas such as AgNP's, they enable the delivery of chemotherapy drugs to the cancerous cell in cancer treatments. In diagnostics, they can detect biological targets thanks to their optical properties and are the number one nanoparticle for labeling DNA or proteins [68].

4.1.2. Nanogels
As the name suggests, nano gels are in a gel-like form. This form provides itself with various advantages. Low viscosity, large surface area, and fast reaction are among the advantages. Nanogels resemble hydrogels in structure. That is, they swell without dissolving in a thermodynamically good solvent [69]. At the same time, thanks to the hydrophilic polymers used in the synthesis stage, they respond to environmental stimuli in the form of reversible volume-phase transitions [70]. These transitions are due to weak molecular bonds. The degree of swelling of nano gels is affected by the osmotic pressure of the medium, so different degrees of swelling can be observed. Which makes nano gels one of the alternative drug carriers [71].

4.1.3. Liposomes
Liposomes, which have recently emerged as carrier antigen agents, can also be used in vaccine deliveries because they are non-toxic and naturally degraded phospholipids [72]. Liposomes not only regulate the antigen release rate but also make them resistant to physical and biological degradation [73].

4.1.4. Nano-emulsions
Nano-emulsions, which attract the attention of researchers most among drug delivery systems, have emerged because of combining two immiscible liquids with the help of an emulsifier [74]. It has succeeded in surpassing nanomaterials due to its high kinetic stability, long-term release profile, improved therapeutic efficacy, good dermis permeability, photosensitive drug delivery, hydrophilicity, and self-assembly. İt is not only used in the field of medicine, but also in areas such as food, cosmetics, and pharmaceuticals [75].

4.1.5. Niosomes
Niosomes are nanocarriers clinically like liposomes. Non-ionic surfactant (NIS) based vesicles, niosomes carrying a nucleus in a bilayer structure, are noteworthy for their regulation of the delivery of amphiphilic agents. The most obvious difference between them and liposomes is that liposomes are composed of phospholipids while niosomes are created from inexpensive NISs. Modifying niosomes with PEG (polyethylene glycol) to increase drug holding capacity and stability is one of the most frequently used methods in recent times [76].

4.1.6. Dendrimers
The dendrimer is a spherical nanoparticle with a 3D structure with hyper-branching. It consists of three main structures: a central core, repeating units, and surface terminal groups [77]. İt is

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physiochemically versatile and functional. These nanoparticles can easily overcome the obstacles encountered in traditional drug delivery mechanisms [59].

4.1.7. Nanosuspension

Nanosuspension is the form of particles smaller than 1 micron colloidally dispersed in water [78]. The solubility of nanosuspensions is high in the aqueous and lipid phases. In this way, nanosuspensions increase the permeability of the brain and reduce the virus load. It does this not only in nanosuspensions but also in nanoemulsions, micelles, nanoparticles, liposomes, and other nanocarrier formulations [79].

4.1.8. Polymer micelles

Polymer micelles have become a nanomaterial that has attracted attention in recent years with their combination without extra support, hydrophobic functional compounds, and the delivery system used in drug transport. Plays an important role in the design and application of micelles in synthetic polymers. Starch is the most suitable biopolymer for a micelle. Starch; ıt has advantages such as low price, easy modification, and more modification methods. But the most popular is starch micelle modified with octanoyl succinyl anhydride (OSA) [80].

4.1.9. Solid lipid nanoparticle (SLN)

Solid lipid nanoparticles (SLN) are made with solid lipids stabilized with surfactants and excipients [81]. Although it is said that SLNs have little toxicity as they are biodegradable, this is still a subject of research. Physicochemical properties such as nanoparticle shape, size, and polydispersity index (PDI) determine the biological activity of SLN [82]. SLNs are involved in transporting lipophilic and hydrophilic substances, drugs, proteins, and genetic material. In addition, SLN also has properties such as increasing the solubility of substances, targeting, drugs promoting and controlling their release [83].

4.1.10. Fullerene and carbon nanotube

Finally, fullerene and carbon nanotubes are included in drug delivery systems. Fullerenes have the most widespread adaptation with the largest C_{60} molecule. This has made fullerenes a sought-after material in various fields of study such as gas storage, drug transport, batteries, and transistors [84,85]. Carbon nanotubes are the dimerization of fullerene molecules found in ‘peapods.

In conclusion, In drug delivery systems, nanocarriers provide advantages in controlling drug release, breaking down drugs, preventing harmful side effects, accumulating the drug in the targeted area, and increasing bioavailability and drug permeability. In addition, while they have positive features such as being able to carry two substances at the same time and being able to move easily in the vessels due to their small size; It also has negative features such as rapid clumping and release before reaching the target area. Today, it is being investigated whether the detected negativities are eliminated and whether there are other disadvantages [58].

4.2. Antimicrobial Applications

Microorganisms are the common name of harmful or harmless living things in micro size. While some of the microorganisms are harmless and even necessary for our survival, some of them are extremely harmful. Studies conducted to neutralize harmful microorganisms are called antimicrobial studies. The resistance of microorganisms to given drugs is called antimicrobial resistance. Antimicrobial resistance is harmful to human and environmental health. Today, the increase in antimicrobial resistance reduces the use of antibiotics and increases the use of more efficient nanomaterials[86].In

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the studies conducted in the past years, it has been learned that metals such as gold, silver, and copper reduce the formation of bacteria. Today, these metals are synthesized as nanoparticles [87]. These nano-sized materials exhibit superior properties compared to their large-scale counterparts. The surface/volume ratio of nano-sized materials varies greatly and, in this case, provides high reactivity.

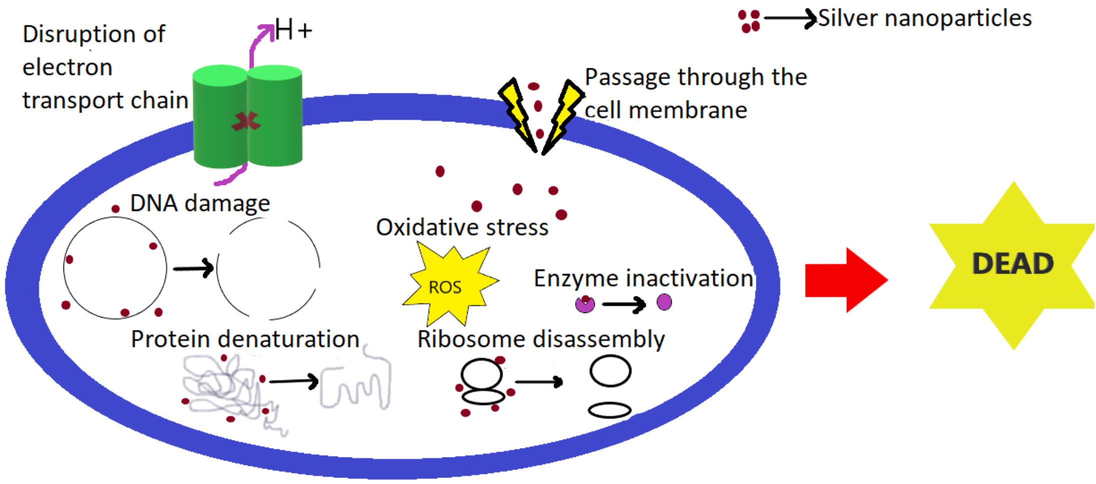

Figure 2. General antimicrobial action mechanism of silver nanoparticles [88].

By examining the morphological and structural changes of metallic silver, silver ions, and silver nanoparticles on bacterial cells, the mechanism is tried to be understood clearly. The mechanism shown in Figure.2 is the working mechanism that has been accepted in the studies conducted so far [89]. Silver nanoparticles adhere to the cell membrane, interact with the proteins in the thiol (-SH) groups, reduce the membrane permeability in that part and enter the cell by replacing the hydrogen cation. AgNPs that enter the cell inactivate enzymes, disrupt protein structures, cause ribosome units to separate from each other, and cause the cell to die by damaging its DNA [23,64].

4.3. Antifungal Drugs

Antifungal drugs are a pharmaceutical fungicide used to treat and prevent serious systemic infections and mycosis (a disease caused by fungi). In general, antifungal drugs can work in two different ways, either by directly killing fungal cells or by preventing the growth and development of fungal cells. These drugs target structures that are required in fungal cells but not in human cells to work. So they fight fungal infection without damaging the body's cells [90].

4.3.1. Types of antifungal drugs

There are several types of antifungal drugs available to combat fungal cells. Some of those; are azoles, polyenes, and echinocandin [91].

Azoles

Triazole and imidazole derivative antifungals are collectively called azole antifungals. They are often used to prevent and treat IFEs. These drugs act by inhibiting the enzyme lanosterol 14α- demethylase and blocking the synthesis of ergosterol, the most important stroller of the fungal cell membrane. In addition, inhibition of ergosterol biosynthesis disrupts the structure of the cytoplasmic membrane, resulting in the loss of essential cell components [90].

Polyenes
Amphotericin B acts by binding to ergosterol and then ruptures the cell membrane, causing the death of the fungal cell by leakage of the resulting intracellular compounds. The interactions of these drugs are due to their pharmacological action on cell membranes. These effects cause undesirable effects by reducing the excretion of the drug or metabolites from the organism [90].

Echinocandin
Echinocandin, a structure not found in mammalian cells, targets the biosynthesis of the fungal cell wall. These drugs are effective against *Candida* species. But they are fungistatic against molds such as *Aspergillus* species [92].

4.3.2. Relationship of antifungal drugs and nanomaterials
Recently, due to the continued growth of life-threatening fungal diseases and the emergence of resistance to developed antifungal drugs, there has been a trend towards synthesizing antifungal nanomaterials with low toxicity and more effective for eukaryotic systems. Antifungal nanomaterials have been developed against life-threatening systemic infections. Another reason for the development of antifungal nanomaterials is to overcome the problems caused by the water insolubility of antifungal drugs used in the treatment of fungal diseases [91].

5. NANOTECHNOLOGY AND CANCER RELATIONSHIP

To understand the relationship between nanotechnological drugs and cancer, we must first understand cancer. Cancer is one of the most difficult diseases to treat worldwide. Despite all the efforts of scientists, the prevalence of cancer is increasing rapidly [93]. The purpose of the production of anti-cancer drugs is to try to stop uncontrolled dividing cells through effective formulations while preserving healthy tissue. Scientists target cells that cannot be stopped non-specifically dividing. Nanotechnology, on the other hand, sheds light on the scientific World for this purpose and produces pharmacologically appropriate paradigms, especially in the production of anti-cancer drugs, the delivery of effective drugs, in the development and production of nano-based implants. Nano based drugs specifically recognize and target diseased cells. Nano-based drugs are on the agenda in diseases that require the continuous release of a drug. Another important activity of nano-based drugs is that they increase the half-life of the drug used and prevent the degradation of enzymes. Nanocarriers have a revolutionary effect against the nasty pharmacological barriers of anticancer drugs by positively affecting the stability and solubility of anticancer drugs [94,95].

5.1. Drug Targeting Approaches

5.1.1. Passive targeting
Intravenous injection is one of the most used methods for nanotechnology-based anticancer drugs. In this type of injection, the aim is to bypass the absorption step that must be done along the intestinal epithelium, allowing the nanocarriers to accumulate in the tumor tissue immediately after disrupting the vascular barrier [93,96].

5.1.2. Active targeting

This method is also referred to as the 'ligand-mediated targeted approach' as it is thought of as the facilitated recruitment of previously targeted cells. There are several specific molecular interaction steps for active targeting [93,96]. The most well-known interactions are receptor-ligand interactions, charge-based interactions, and chemical affinity. Thanks to the active targeting approach, target cells recognize nanoparticles and improve drug distribution, and proteins, sugars, or lipids in organs, even molecules secreted by tumor cells, can be target substrates [96]. There are differences in substrate molecules between normal and diseased cells, and targeting approaches achieve results by taking advantage of these differences [93].

5.1.3. Critical aspects of targeting systems

There are some points to be considered in the use of the targeting system. One of them is the conjugation of ligands on the nanoparticle. Because the density of these ligands is directly proportional to the strength of the substrate activity. Although the covalent conjugation process is mostly preferred, physical absorption applications using affinity complexes are also used effectively. The critical issue to consider is maintaining the stability of conjugated drugs exposed to adverse environments. Attention to payload capacity and targeting freedom is crucial to increase in vivo efficacy in nanoparticle-based active targeting systems.

5.1.4. Release strategy in nano-based drugs

The effective packaging of the drug used depends on the load-carrying capacity of the drug. The packaging term in question depends on how efficient the conjugation of the drug is. In nano-systems, there are 2 different systems determined according to the activation factors of drug release. These systems are open-loop and closed-loop systems. In open-loop control systems, the factors that stimulate drug release are electric fields, magnetic-acoustic pulses, and thermal factors. In closed-loop control systems, the drug release rate changes depending on the presence and intensity of the stimulus in the targeted area [93,96].

6. ECOLOGICAL SAFETY AND EFFECTS IN NANOMATERIALS

6.1. Unseen Dangers in Nanotechnology

Today, thanks to nanotechnology, millions of products are ordered for sale on market shelves. Now, some products produced with nanotechnology have side effects. These side effects are harmful to both food and the environment. Today, scientists have examined whether nanotechnological structures have side effects or risks. As a result of the studies carried out, effects against ecology were found.

6.2. Effects of Nanoparticles on Human Health

How nanoparticles enter the human body is known as respiration, skin, and nutrition. Nanoparticles entering the body can easily pass into the blood [97]. Many organs of the body are targeted and the most affected target area because of respiration is usually the lungs. When gaseous nanoparticles are inhaled into the lungs, they reach the outer membrane of the chest wall (parietal pleura). It is inactivated by being surrounded by macrophages of short size. It has been suggested that the toxic effect of vapor and gaseous nanoparticles reach the lungs through the respiratory system and other systems and that the effect is pulmonary and systemic inflammation [98]. According to this idea, it has been reported that pulmonary endothelial dysfunction resulting from inflammation, platelet activation, stimulation of thrombotic factors, atherosclerotic plaque lesion and rupture, vascular endothelial dysfunction, stimulation of lung and liver reflexes, disturbance in heart rate and rhythm and even sudden cardiac arrest may result.

6.3. Effect of Nanomaterials on the Environment

With the increase in the production of nanomaterials, the effect on people and the environment is increasing. The residues of nanoparticles mostly reach us by reaching the water, then the soil, and from the soil to the plant. As a result of an experiment performed on freshwater creatures, the effect of nanoparticle wastes on aquatic organisms was investigated [99]. It is known that ecotoxicity tests on vertebrates, fish, artemia, and algae create a low hazardous potential on living things.

As mentioned in the scope of the study, nanomaterials are used in many application areas in the field of health. At this point, although nanomaterials promise useful features that shed light on the future, it is seen that there are some disadvantages as well. Especially in terms of human health, it is known that nanoparticles can easily pass into the blood in the body. At this point, developments continue, and it is seen that important results will be obtained in the treatment of many diseases, especially in the field of health, as a result of eliminating the disadvantages. Within the scope of the study, it has been seen that nanomaterials are very important in terms of human health as well as in the advancement and development of technology and it is of great importance to increase their studies.

7. CONCLUSION

The fact that nanomaterials can be applied in many areas rapidly increases the prevalence of nanomaterial production. At this point, many technological and biotechnological products are developed. Within the scope of the study, the properties, production, and application areas of nanomaterials needed for these developments are mentioned. Studies have shown that there are many production methods in the production of nanomaterials and that chemical methods are harmful to the environment. At this point, it is seen that the green synthesis method is more promising in terms of reducing the damages since it is an environmentally friendly method. In addition, it is seen that the use of nanomaterials for drug delivery systems, antibacterial and cancer cells is important and used in many applications. At this point, although it is aimed to send the transported drug directly to the target region, studies are continuing on the production of nanomaterials that can overcome the obstacles encountered while being sent to the target region. It has also been observed that nanomaterials give very good results in antibacterial applications and Ag metal is the most preferred in these applications. The obtained research has shown that nanomaterials provide significant improvements in many aspects such as drugs, sensors, and antibacterial and anticancer applications in the health sector. These results show that nanomaterials are promising in the advancement and development of biotechnology and that increasing studies are of great importance.

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