World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(Research Article)

Silver nanoparticles in medicine and technology: Synthesis, functionality and future prospects

Vrushali Satpute and Dnyaneshwari Sawant *

Vidya Niketan Collage of Pharmacy, Lakhewadi, Indapur, Pune, Maharashtra 413103, India.

World Journal of Advanced Research and Reviews, 2024, 24(01), 1502–1516

Publication history: Received on 05 September 2024; revised on 13 October 2024; accepted on 16 October 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.24.1.3138

Abstract

Nanomaterials, particularly nanoparticles (NPs), have emerged as forefront materials of the 21st century due to their unique properties and potential applications. Silver nanoparticles (AgNPs) are among the most attractive inorganic nanomaterials, widely used due to their significant antibacterial properties, broad-spectrum activity, and potential applications across various fields, including health, food storage, textiles, and environmental solutions. AgNPs exhibit a large surface-area-to-volume ratio, enabling enhanced interaction with bacterial cells, making them effective in medical and industrial applications. Despite concerns over their toxicity, AgNP-based products have been approved by multiple regulatory bodies.

Nanoparticle synthesis methods are generally divided into physical, chemical, and biological approaches. Although physical and chemical methods are efficient, they involve toxic chemicals and energy-intensive processes. Biosynthesis, particularly plant-based, offers an eco-friendly alternative, reducing the environmental and health risks associated with chemical agents. The review also explores the therapeutic potential of AgNPs in drug delivery systems, especially in topical formulations like nanoemulsions, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs). These nanocarriers enhance drug stability, skin penetration, and controlled release, making them ideal for dermal and transdermal delivery.

Moreover, the use of AgNPs in dentistry is highlighted for their bactericidal properties, which help prevent infections and implant failure, with the potential for enhancing therapeutic outcomes without common drawbacks like tooth staining. Overall, AgNPs exhibit promising applications in biomedical, pharmaceutical, and dental fields, and their novel functionalities continue to advance the development of nanotechnology-driven solutions.

Keywords: silver nanoparticles (AgNPs); nanoparticles (NPs); Topical drug delivery system (TDDS); small unilamellar vesicles (SUV); multi-lamellar vesicles (MLV); silverdiamine fluoride (SDF); localized surface plasmon resonance (LSPR); skin discoloration (argyria); vascular endothelial growth factor (VEGF).

1. Introduction

In recent decades, nanomaterials (NPs) have emerged as one of the most innovative materials. They have been dubbed the "material of the 21st century" due to their distinct designs and combinations of properties that set them apart from traditional materials [1]. The term "nano" denotes a billionth of a meter, or 10^{-9} [2]. Two general categories for nanoparticles are (i) inorganic and (ii) organic. Organic nanoparticles include carbon nanoparticles (like fullerenes, quantum dots, and carbon nano tubes), whereas inorganic nanoparticles include semi-conductor nanoparticles (like Zn O, ZnS, and CD's), metallic nanoparticles (like Au, Ag, Cu, and Al), and magnetic nanoparticles (like Co, Fe, and Ni). Nanoparticles of gold and silver (noble metals) offer exceptional properties and practical flexibility [3].

---

* Corresponding author: Dnyaneshwari Sawant

Because of its broad range of activity against pathogens like bacteria, viruses, fungus, andprotozoa, silver has also been utilized extensively as a universal medicinal agent. Since antibiotics were developed and Alexander Fleming discovered penicillin in 1928, the useof silver was restricted because of the exorbitant expense of producing it. Antibiotic treatment is currently widely used. Overuse of antibiotics, which is frequently insufficientto treat dental conditions, leads to the emergence of resistant bacterial strains such as Bacillus amyoliquefaciens [4, 5].

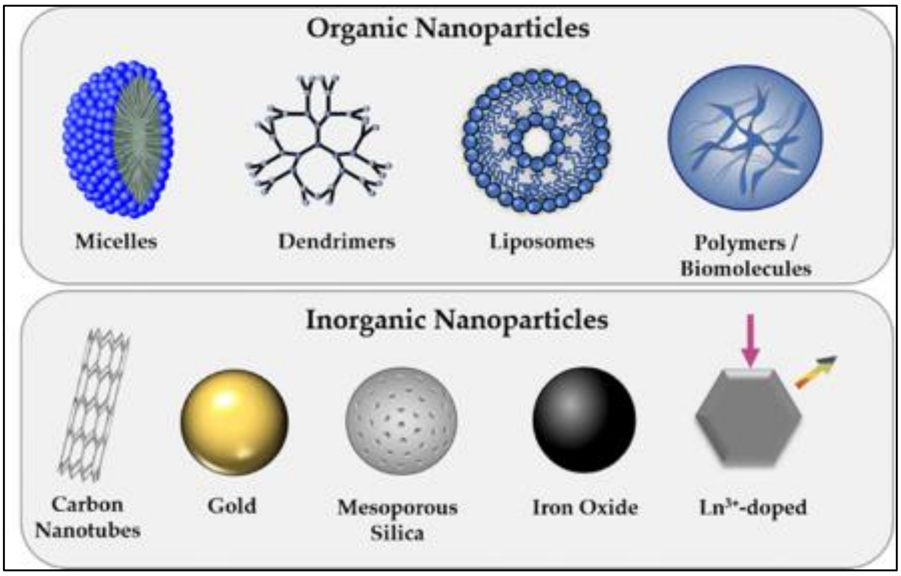

Figure 1 Overview of commonly used nanoparticle (NP) types, classified as organic, inorganic, or composite structure

Silver nanocrystals, which are primarily hydrosols, are among the most appealing inorganic materials due to their many uses in photography [6]. AgNPs are a type of zero-dimensional materials that range in size from 1 nm to 100 nm and have unique morphologies [7]. The availability of increased surface area is primarily responsible for the high efficiency of silver nanoparticles.

Compared to micro-sized silver ions, the area to volume ratio for interactions facilitatesthe penetration and disruption of nanoparticles into the bacterial cells.[8]

AgNPs have found widespread use as anti-bacterial agents in a variety of environmental applications, food storage, textile coatings, and the health sector. It is significant to remember that there is still uncertainty regarding the toxicity of silver, even after decadesof use. Numerous recognized organizations, such as the US FDA, US EPA, SIAA of Japan, Korea's Testing and Research Institute for Chemical Industry, and FITI Testing and Research Institute, have authorized products created with AgNPs.[9]

Drug items used for local action or systemic effects are the two types that are dermally given through the skin. Applying something on or near the skin's surface can have a localized effect on the stratum corneum or alter the function of the epidermis or dermis. Local actions include gels, creams, ointments, pastes, suspensions, lotions, foams, sprays, aerosols, and solutions. Yetisen and associates. [10]

2. Synthesis of nanoparticals

2.1. Synthesis of AgNPs Using Physical And Chemical Methods-

Silver nanoparticles are generally synthesized via physical, chemical, and biological techniques. But many of these techniques involve hazardous, farmable, and difficult- to-remove chemicals that endanger both people and the environment [10,11]. One approach that appears to be promising for producing nanoparticles quickly, easily, safely, economically, and environmentally is biosynthesis [12,13, 14].

The benefits of physical approaches include speed, the use of radiation as a reducing agent, and the absence of toxic chemicals; however, the drawbacks include high energyconsumption and low yield, solvent contamination, and non-uniform distribution [15–19].Silver nanoparticles are prepared chemically using either water or organic solvents [20, 21]. AgNP Synthesis Metal precursors, reducing agents, and stabilizing orcapping agents are needed in the solution. Reducing agents that are frequently utilized include sodium citrate, alcohol, borohydride, ascorbic acid, and hydrazine compounds.The Prasines and Sotiriou approach.[22]

Various biomedical sectors have employed a variety of silver nanostructures with unique features [23]. A wide range of products, including electronic devices, paints,coatings, soaps, detergents, bandages, etc., have used silver nanoparticles of varioussizes and forms [24].

Therefore, it is essential to consider certain physical, optical, and chemical characteristics of silver nanoparticles in order to maximize their utility in these applications. Surface property, size distribution, apparent morphology, particle composition, dissolution rate (i.e., reactivity in solution and efficiency of ion release), and types of reducing and capping agents used are all significant details of the materialsto take into account during their synthesis. The two primary ways for synthesizing metalnanoparticles (NPs) are top-down and bottom-up, as seen in Figure 2. The top-down method excludes bulk materials. The bottom-up approach creates nano-sized materials by assembling individual atoms and molecules into larger nanostructures in order to create the necessary nanostructures [25].

Nanotechnology uses the findings of nanoscience to create novel materials and usefulinfrastructure. Currently, one of the primary areas of nanoscience that is expanding isnanochemistry [26].

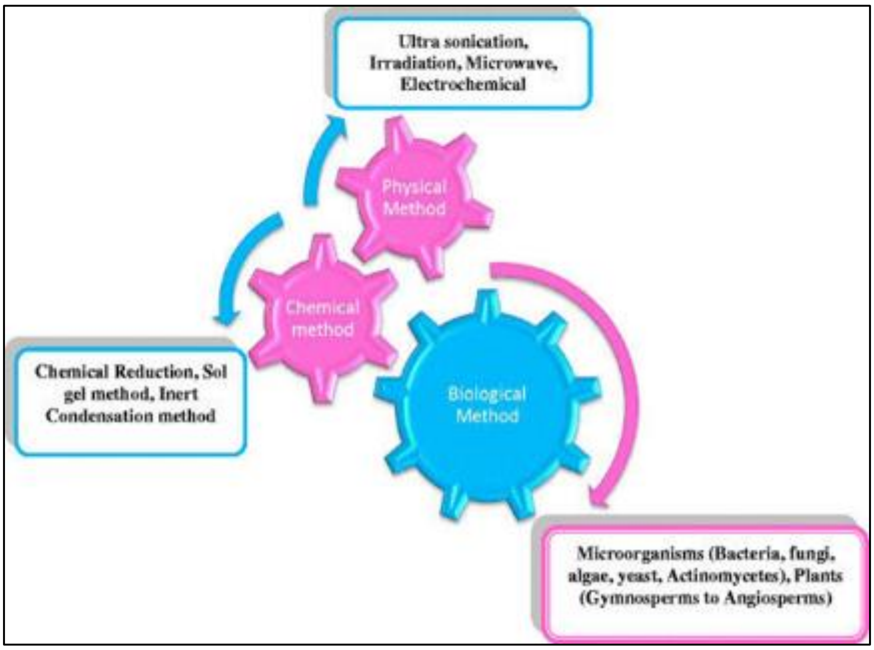

Figure 2 Methodes involved in nanoparticles synthasis

2.2. Synthasis Of Agnp Using Biological Methode

A great deal of interest has been shown in the biosynthesis of nanoparticles, particularly silver nanomaterials, from organic or plant extracts due to their manyuses and diverse array of bioactive reducing metabolites. It is well recognized thatplants are a very desirable source for creating nanoparticles. Plants are more resistant to metal toxicity than bacteria and algae, making them a more environmentally friendly option for producing silver nanoparticles [27, 28].

Because they are the source of photosynthesis and have more available Hp ions tolessen the production of silver nitrate within the silver nanoparticles, green leavesare utilized and preferred in this instance over other plants when producing silvernanoparticles. Ephedra intermedia stem extract has been effectively used to develop green synthesis of silver nanoparticles (Ag NPs). To find the ideal circumstances, the impact of reaction temperature, amount of stem extract, and concentration of silver precursor on the bio-reduction reaction was assessed. It was discovered that the natural carbohydrates found in Ephedra intermedia functioned as efficient reducing and capping agents during the production of AgNPs [29].

Therefore, there are certain drawbacks to creating Ag NPs chemically, includingthe fact that they are hazardous to human health and the environment and, moreimportantly, that they damage many normal cells, which could lead to major issues. Silver, however, was discovered to have distinct impacts on a range of cultivated cells.

Only silver exhibited notable cytotoxicity as compared to other metals; nevertheless, lowering aberrant cellular activity (characterized by asymmetrical forms and morphology) and raising the dosage of silver can cause cellular shrinkage. When synthesizing Ag NPs, biological agents are preferable over chemical ones because they are more economical, environmentally friendly, and use fewer hazardous reagents and solvents, which can reduce toxicity and increase material energy efficiency [30]. Because harmful bacteria have the potential to infect the nanoparticles utilized in medical areas, using plant extract for nanoparticle synthesis has been shown to have more advantages than microbial procedures [31].

Here, the most discussed nanomaterials in terms of exposure analysis and hazard assessment are listed in A selection of representative nanomaterials are presented based on their primary applications and intrinsic physicochemical characteristics through a classification of nanomaterial compositions. Although they are frequently utilized as comparatively "inert" nanoparticles for comparison purposesin the context of environmental nanotoxicology, gold nanoparticles (Au NPs), which are recognized as one of the most significant materials with potential for usage in biomedical disciplines, are not included in [32].

3. Novelty of silver nanoparticals

Nanotechnology is an emerging field of science that mainly deals with nanomaterialsto overcome size limitations and change the world perspective on science. It has revolutionized agriculture sectors and played essential roles in various fields like agricultural biotechnology, food security, and crop production. Nanoparticles distinct physicochemical features are extremely helpful in inducing plant metabolism.

However, their interactions with plants have not been clarified and understood in detail. Several contradicting reports of nanoparticles regarding accumulation, translocation, absorption, biotransformation, and toxicity were reported in diverse plant species. AgNPs are one of the most significant nanomaterials whose impacts arestill under Figure 3 Nanoparticles as novel topical drug delivery system (TDDS) usedto improve skin penetration, dermal and transdermal delivery investigation [33,34].

The use of metal nanoparticles is not limited to molecular detection; recently, AgNPshave been used as delivery vehicles for therapeutic agents, including antisense oligonucleotides and other small molecules. Noble metal nanoparticles have specific high developed photophysical properties which contribute to their potential as photoactivated drug delivery vectors. AgNPs have been used extensively as biologicalsensors which take advantage of plasmon resonance (PR) to enhance detection of specific targets. Noble metal nanoparticles based sensors benefit from the extreme sensitivity of localized surface plasmon resonance (LSPR) spectra to environmental changes.

Modifiable in size and shape, high-density surface ligand attachment, improved stability of surface-bound nucleic acids, transmembrane delivery without harsh transfection agents, defense against therapeutic degradation, and potential for better timed/controlled intracellular release are just a few of the many benefits that small metal nanoparticles (NPs) offer as drug carriers. AgNPs' photophysical characteristicshave the potential to advance drug delivery by facilitating targeted administration, spatiotemporally regulated (photo)release, and imaging-based delivery confirmation.[35]

Colloidal systems with an average diameter of less than 500 nanometers are referred toas nanocarriers.[36]Dermal and transdermal drug delivery has been the main focus of research on novel nanocarriers, including microemulsion, liposome, and nanoparticulate carriers. As topical drug delivery systems, nanoparticles offer numerous benefits, including increased drug deposition in the target area, improved drug loading stability in the form of greater physicochemical stability, and sustained and regulated drug administration from nanoparticulate systems. Lipid-based nanoparticles, including liposomes, niosomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), were extensively studied as topical drug deliverymethods in the literature. To accomplish cutaneous and transdermal drug administration, other materials such as polymeric nanoparticles, metal nanoparticles, nanocrystals, and nanospheres ,as seen in Figure 3,were also explored.[37]

Hair follicles are a viable route for augmenting dermal and transdermal administration penetration into the skin. Regardless of the kind of nanoparticles, the most crucial factorthat could influence the depth of follicular penetration is their average diameter.[38] Targeting individual hair follicles specifically may be a fantastic way to treat hirsutism, androgenetic alopecia, and acne vulgaris. The benefits of trans-follicular drug delivery include tissue targeting, deep penetration into epidermal layers, long-term drug deposition and storage, and increased cutaneous bioavailability.Nevertheless, there are anumber of difficulties with transdermal administration via hair follicles.[39]

such as inadequate transdermal delivery system characteristics (adhesion, permeability, storage, shelf life, etc.), biological factors (site of application and variability in skin permeation), and poor physicochemical properties of active pharmaceuticals (solubility,pharmacokinetics, metabolism, compatibility, etc.) that need to be addressed.[40]

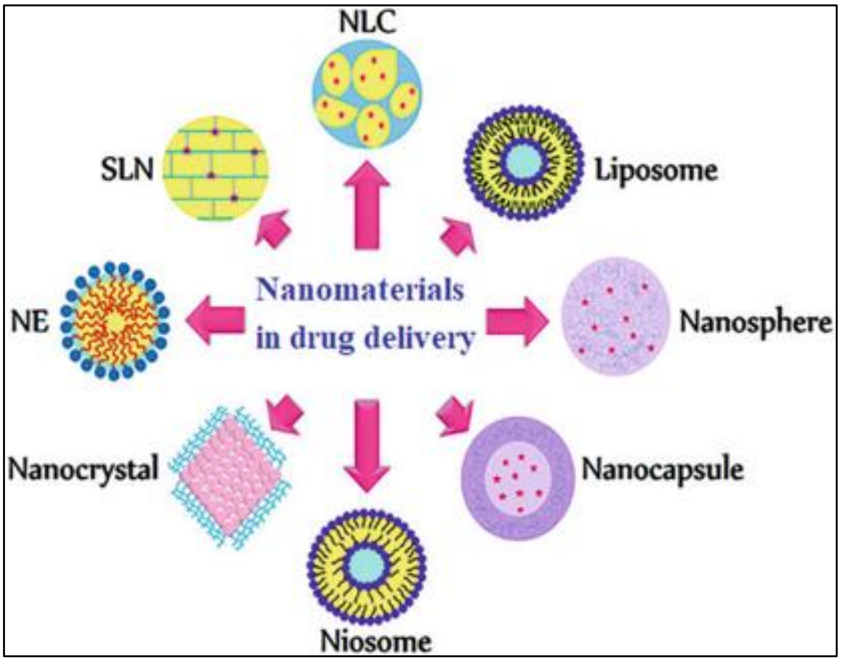

Figure 3 Nanoparticles as novel topical drug delivery system (TDDS) used to improveskin penetration, dermal and transdermal delivery

3.1. Nanoemulsions (NEs)

With their translucent nature, smooth skin feel, regulated and prolonged drug release, simplicity of self-administration, and lack of gastrointestinal side effects, NEs are alsopromising nanocarriers for transdermal drug delivery to systemic circulation.[41]

Through a variety of methods, including an increase in the drug's solubility in thecarrier, carrier uptake into the stratum corneum and fluidization, and changes and dissolution of the stratum corneum lipids, NE containing penetration enhancers mayboost skin penetration.Hydrophilic and lipophilic drug distribution can be enhancedtransdermally by NEs containing oils and surfactants in their formulations.[42]

3.2. Solid Lipid Nanoparticles (SLNs)

The first class of lipid-based nanocarriers made of solid lipids and emulsifiers are called solid lipid nanoparticles (SLNs). They are made from lipids that, at normal temperature, are totally solid. [43]Topical drug delivery systems, or SLNs, possess the ability to be both adhesive and occlusive. This allows them to create a uniform and homogenous layeron the stratum corneum, prolong their residence time, and improve skin penetration by interacting with the skin's layers and altering their barrier properties.In comparison to freemedications for the treatment of psoriasis, a reported study shown that SLNs could greatly improve the amount and depth of cyclosporine A and calcipotriol skin penetration.[44]

3.3. Nanostructured Lipid Carriers (NLCs)

The second generation of lipid nanoparticles, known as NLCs, are made up of a combination of liquid and solid lipids. These nanoparticles show promise as delivery vehicles for cosmetics and pharmaceuticals, including follicular, transdermal, and dermalapplications. Drug protection, regulated drug release, increased drug bioavailability, and improved skin penetration and deposition are just a few benefits of using these kinds of nanocarriers.By preventing trans-epidermal water loss and forming a film at the stratum corneum's surface, NLCs can help improve skin moisture.For the treatment of androgenicskin conditions such acne, hirsutism, and alopecia, follicular distribution of active medicines is another exciting use for lipid nanoparticles, particularly NLCs. The size of the nanoparticles is the primary determinant affecting the quantity and depth of folliculardelivery [45].

3.4. Liposomes

A vesicle known as a liposome is made up of one or more lipid bilayers with an embedded aqueous phase. Liposomes typically contain cholesterol and phospholipids. Fortopical medication administration, liposomes vesicular nanocarriers offer a number of benefits, including regulated release of the drug, targeted drug deposition in skin layers, decreased systemic absorption, and fewer adverse effects. Lower serum concentrations and drug excretion in urine were used as evidence of localized skin deposition of active medicines loaded liposomes.[46]

Particle size, fluidity, lamellarity, occlusive qualities, and liposome types and compositions all have a significant impact on the drug-loaded liposome's depositionefficiency.

Smaller liposomes have been shown to penetrate deeper into the skin layers, and smallunilamellar vesicles (SUV) have been shown to increase skin penetration more than multi-lamellar vesicles (MLV). These findings highlight the importance of liposome particle size in skin penetration.[47]

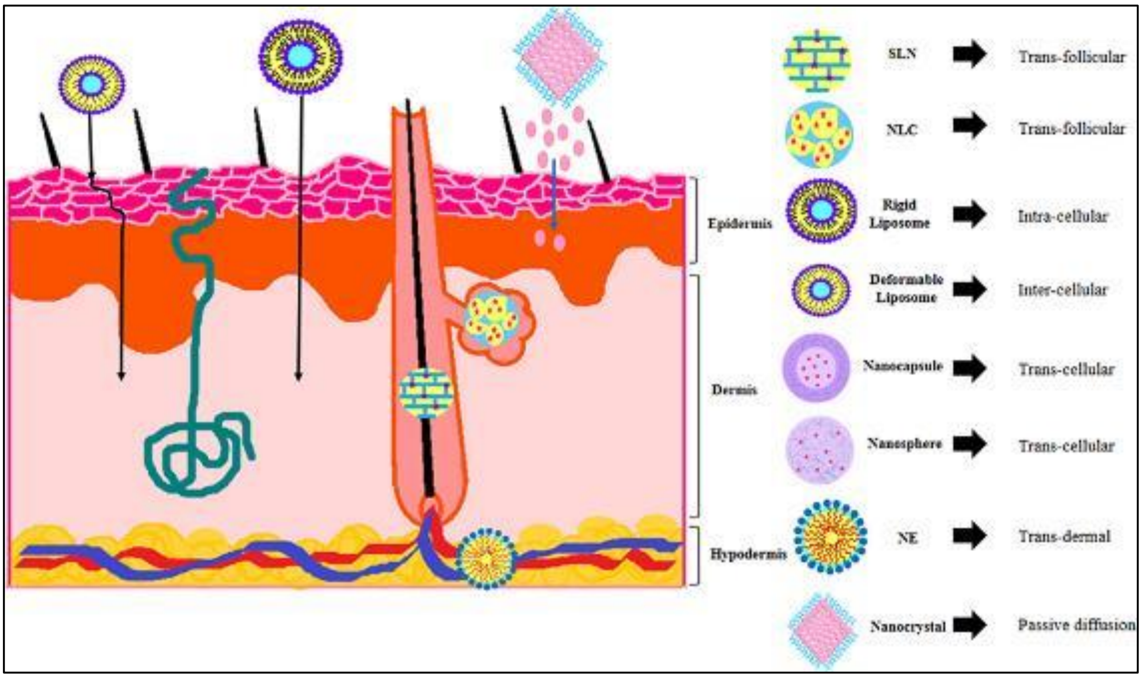

Figure 4 A schematic view of different nanocarriers mechanisms in skinpermeation enhancement and targeted delivery to skin organelles

3.5. Niosomes

The other kind of vesicular drug delivery system has a spheroidal form and can be one ormore layers deep. These are called niosomes. They are created when molecules that are amphiphilic come together. Niosomes are vesicular drug delivery systems made of nonionic surfactant that are presented as an alternative to traditional liposomes.[48] Niosomes are useful as nanocarriers for proteins, peptides, and chemical medications.One crucial factor impacting niosome-mediated transdermal drug distribution is the fluidity ofthe vesicular membrane. Essential oils ,particularly terpenes , play a significant role in niosome compositions because they can improve penetration by upsetting the structure ofthe stratum corneum. Additionally, essential oils may improve the niosomes' flexibility and facilitate vesicle fluidization, both of which may improve transdermal medicationdelivery.[49]

3.6. Nanocrystals

Particulate systems called nanocrystals are made completely of medication. The size of their particles varies from 1 to 1000 nm. Although the most significant disadvantage is the requirement for frequent dose administration, nanocrystals are appropriate drug delivery systems for essentially insoluble active pharmaceuticals, medications with limited skin penetration, and less bioactive compounds. According to a study, dexamethasone-loaded ethyl cellulose nanocarriers and regular dexamethasone cream did not improve skin penetration as much as dexamethasone nanocrystals. Furthermore, compared to conventional or ethyl cellulose nanocarrier formulations, where the majority of the drug remained in the epidermis, the results showed that in the nanocrystalformulation, the majority of the medication was accumulated in the dermis layer.

Additionally, the use of nanocrystal formulation resulted in faster skin penetration.[50]

4. Mode ofaction and applications

4.1. Dental application

In order to prevent the pathogenic contamination of dental implants,proper tooth-brushing techniques, prophylactic antibiotics, and antimicrobial mouthwashes are specifically recommend major goal in dentistry is to provide the proper protection of the oral cavity, which represents a pathogenic-susceptible gateway for the entire body . Biofilms developed on dental implant surfaces may additionally cause inflammatory lesions on the peri- implant mucosa, thus increasingthe risk of implant failure .

Adding silver-based nanostructures to or altering common dental materials is an appealing tactic that dentists around the world are using to give them extra bactericidalbenefits. While silver, in the form of nano silverdiamine fluoride (SDF), has beneficialeffects in caries prophylaxis, there are drawbacks to using this specific molecule, withtooth discoloration being one of the most obvious. The use of nano silver could stop black staining in teeth, which typically happens after app-based sensors take advantageof the extremely sensitive localized surface plasmon resonance (LSPR) spectra to environmental changes. By significantly increasing the contact surface, AgNPs' antimicrobial properties would be enhanced. Metal nanoparticle application is not An attractive strategy embraced by worldwide practitioners in order to provide additionalbactericidal effects to general-use dental materials is to modify or embed them with silver-based nanostructures . Though silver has favorable effects in caries prophylaxis in the form of nano silverdiamine fluoride (SDF), the use of this particularcompound has some disadvantages, one of themost noticeable effects being represented by tooth staining By reducing the size of AgNPs,the contact surface will be considerably increased; in this way, the antimicrobial effects of silver would be improved, and the use of nano silver could prevent black staining in teeth, which usually occurs after the app based sensors benefit from the extreme sensitivity of localized surface plasmon resonance (LSPR) spectra to environmental changes.Application of metal nanoparticles is not limited to molecular detection.

Recently, AgNPs have been harnessed as delivery vehicles for therapeutic agents, including antisense oligonucleotides and other small molecules. Small metal NPs offermany advantages as drug carriers, including adjustable size and shape, enhanced stability of surface-bound nucleic acids, high-density surface ligand attachment, transmembrane delivery without harsh transfection agents, protection of the attached therapeutic from degradation, and potential for improved timed/controlled intracellular release. The photophysical properties of AgNPs may potentially bring these to the forefront of drug delivery, enabling targeted delivery, spatiotemporally controlled (photo-)release, and delivery confirmation via imaging lication of SDF [51]

4.2. Antibiotic application

An alarming phenomenon of current healthcare practice is the occurrence of many drug- resistant microorganisms, which leads to ineffective conventional monotherapy. Bacterialinfections and them related complications represent a major and frequent cause of death .

With the aim to overcome the limitations that occurred due to drug-resistant pathogens, worldwide research focused on the investigation of antibacterial resistance mechanisms, as well as on the development and optimization of unconventional and effective antibacterial strategies. Silver-based compounds have been used as antimicrobial agents for thousands of years,proving the ability to go through biological membranes and to exhibit local or systemiceffects, thus being used for different treatments, including dental and digestive pathologies, wounds and burns healing.

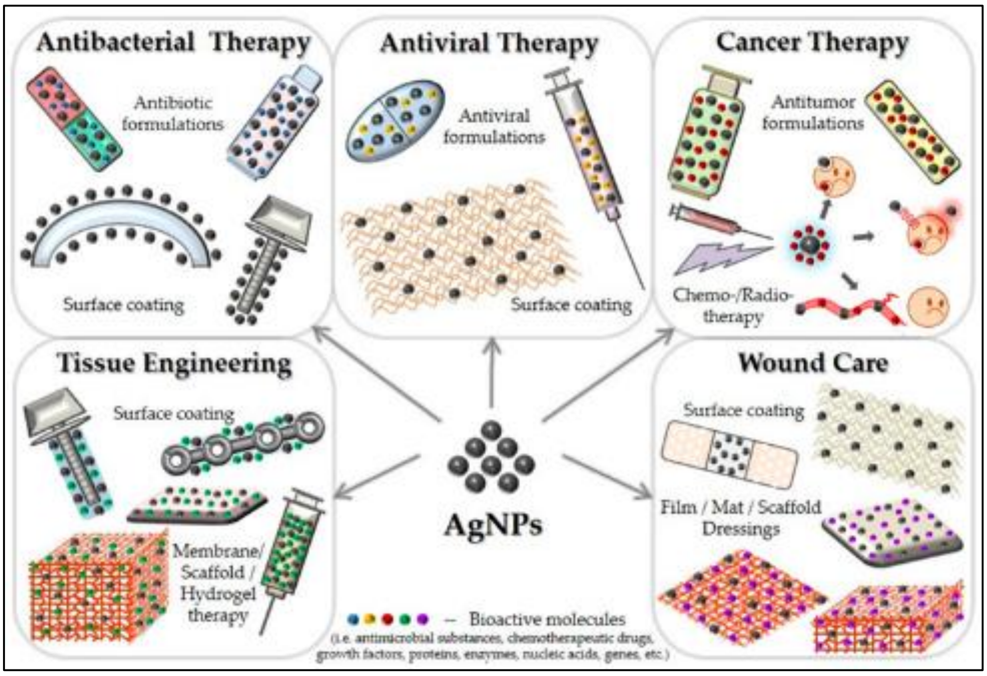

Figure 5 Applications of silver nanoparticles (AgNPs)

Despite their remarkable therapeutic properties, the weakness of such compounds is related to their toxicity on human cells, which occur at higher concentrations. In addition, if prolonged treatment with silver-based compounds is applied, their accumulation in the organism may lead to vital organs' impairment and skin discoloration (argyria). Therefore, to overcome cytotoxicity, products containing silver compounds and nanoparticles require very low metallic concentrations and suitable delivery systems.Ag NPs exert their activity through several Antibacterial mechanisms which reduce the Possibility of resistance development to Ag NPs. Ag is dissolved in aqueous solution forming Ag + Ions which act as antimicrobial agent (Fig 5). One Of theantibacterial mechanisms of Ag + ions is due To their interaction with sulfur phosphorus Groups in the structure of proteins of the cell walland plasma membrane of bacteria which lead to Dysfunction of these proteins thereby threatning Organisms life [52].

On the other hand, silver ions Bind to negatively charged parts of the membrane Thus creating holes in the membrane, causing Cytoplasmic contents flowing out of the cell, Therefore the proton gradient dissipates across The membrane and finally cause cell death [53]. Thereafter, existence of silver ions inside the cell Can disturb the function of electron transport chain Of the bacteria. SilverAg + ions also bind to DNAAnd RNA ofthe bacteria and inhibit cell division [54]

Chemically synthesized spherical AgNPs showed more effective killing bacteria ability Than rod-shaped counterparts when used against both Gram-negativeand Gram-positive pathogens.It was evidenced that the antibacterial activity of nanosilver is strongly related to their microstructure, Namely the presence of (1 1 1)crystallographic plane [55]

4.3. Antiviral application

The intrinsic antiviral mechanism of silver nanoparticles is not completely known and understood, the studies requiring more complex structural, molecular andimmunological research than in the case of antibacterial properties. In a similar way withtheir antibacterial activity, the antiviral effects induced by AgNPs rely on the specific affinity for essential biomolecules (viral proteins and glycoproteins, enzymes, lipids, nucleic acids) and Ag+-mediated biostatic events, such as obstruction of cellular attachment and invasion, the arrest of intracellular viral replication or propagation, hinder of extracellular virions production .

Nano silver-based formulations proved efficient therapeutic effects against several pathologies caused by clinically relevant viruses, such as severe acute respiratory syndrome coronavirus , human papilloma virus (HPV) , rotavirus and other enteric VirusesIt is worth mentioning that new and effective platforms containing AgNPs were evaluated for their biocidal activity against viral vectors, generally mosquito- borne pathogens including Zika virus , Dengue virus ,West Nile virus and Chikungunya virus [56].

The intrinsic antiviral mechanism of silver nanoparticles is not completely known and understood, the studies requiring more complex structural, molecular andimmunological research than in the case of antibacterial properties. In a similar way withtheir antibacterial activity, the antiviral effects induced by AgNPs rely on the specific affinity for essential biomolecules (viral proteins and glycoproteins, enzymes, lipids, nucleic acids) and Ag+-mediated biostatic events, such as obstruction of cellular attachment and invasion, the arrest of intracellular viral replication or propagation, hinder of extracellular virions production. [57].

4.4. Cancer Therapy

Many studies have shown that silver nanoparticles have made their way into therapeutic applications in cancer as anti-cancer agents . Several in vitro studies have indicated that silver nanoparticles can enter cells by endocytosis and their localization inside the cecal be determined as the perinuclear space of cytoplasm and endo-lysosoma compartment . Besides, silver nanoparticles can enter the mitochondria and produce reactive oxygen species (ROS) by affecting the respiration of cells. In summary, the mechanisms of AgNPs as toxic can lead to DNA damage, oxidative stress, induction of apoptosis, and mitochondrial damage to cancer cells.The mechanism of action of silver nanoparticles on cancer cells is schematized in (figure .6). Furthermore, there are studies that AgNPs affect the function of the vascular endothelial growth factor (VEGF). It is also known as vascular permeability factor and plays a major role in the angiogenesis within tumors . These results support AgNPs have anti-cancer properties that can be used as an alternative for cancer therapy and angiogenesis inhibitor therapy.

Theranostic applications of green- synthesized nanoparticles were investigated for biologically compatible and potential approaches in biomedical field (antimicrobial, anti- inflammatory, antinociceptive, anticancer and enzyme inhibition activities).

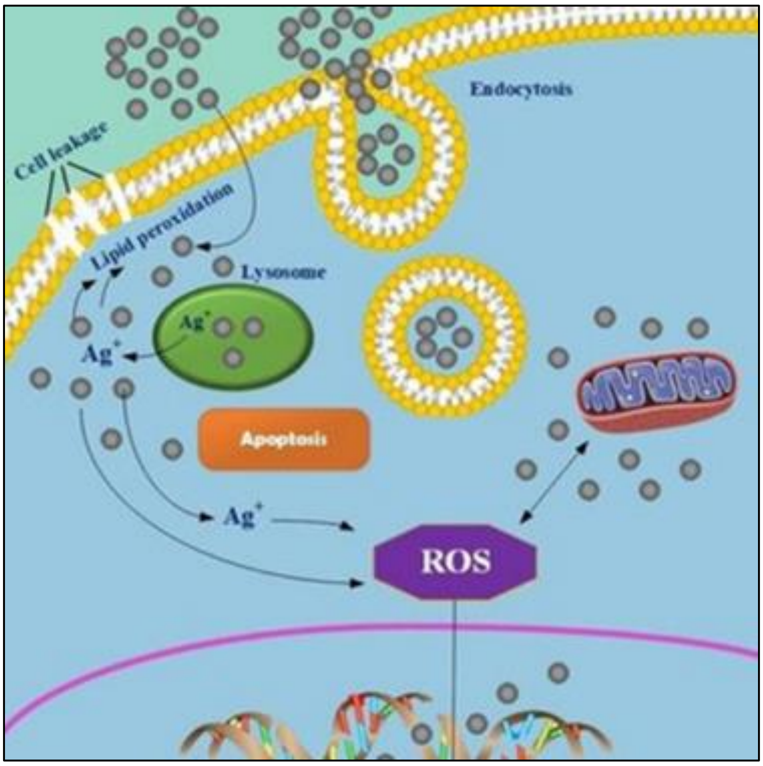

Figure 6 Schematic representation of the mechanism of anticancer effect of silver nanoparticles

Theranostic is defined a combination of diagnostics and therapy. The bio-synthesized AgNPs could be used in theranostic applications including anti-cancer therapeutic agent, drug delivery and bioimaging vehicle. Green AgNPs can be used as beneficialtheranostic agents for further discovery of various biomedical applications [58-59]. AgNPs, which were biosynthesized with various applications, were tested in different cancer cell lines. summarizes the recent studies comparing potential therapeutic approaches of AgNPs on different cancer types. Currently, theproduction of many toxicological data related to nanoparticles occasionally causes an adverse perception of their use Nevertheless, toxicity may be helpfulin cancer treatments because the cytotoxic effect is desirable for cancer cells. Many studies suggest that positive results have been obtained when incorporating silver nanoparticles into cancer therapies. New properties of silvernanoparticles and rapidly changing new application fields are emerging along with the increase in the number of scientific studies. In particular, the development of different techniques for the synthesis of silver nanoparticles leads to enlarge the application fields in medicine. It is thought that silver nanoparticles produced by green biosynthesis using plant extracts or microorganisms may be more suited to clinical approaches than the physical or chemical methods. Additionally, green Biosynthesis of AgNPs is a simple, safe,cost effective and eco friendly approach. Because of all these reasons, green silver nanoparticles seems to be a promising an anti-cancer agent in the field of medicine. But, further researches need to enhance its selectivity on cancer cells,and to determine biocompatibility and side effect in animal models. [60]

4.5. Wound healing

Damage to the skin's and the surrounding tissues' natural structure is referred toas a wound. This type of damage can result from a variety of stressors, such as mechanical or physical harm, chemical or thermal damage, or biological impairment. Immediately following the occurrence of a wound, the natural healing process begins with the remarkable local recruitment of immunological, cellular, and vascular components that work in concert to properly restore structural and physiological functioning [61,62]. The proper order of the following crucial steps is necessary for this process to occur: tissueremodeling, cellular proliferation, re-epithelialization, hemostasis, and inflammation [63, 64]. The wound healing process is insufficient when the afflicted tissue is unable to heal adequately, which can result in a number of complications and even fatal disorders. There aren't many approaches accessibleright now for the clinical care of wounds. For example, skin autografts and xenografts offer a superior healing process and compatibility.

A Ideal treatment option for deep wounds. These tactics have several drawbacks in addition to being costly, like limited bioavailability, heightened immunogenicity, and heightened potential for disease transmission [65, 66]. Furthermore, oxygen-enriched therapy helps hasten wound healing since oxygen is necessary for the induction of angiogenesis, the stimulation of collagen production, and subsequent re-epithelialization . In addition to being an expensive and difficult process, hyperbaric oxygen therapy was found to have limited effectiveness since negative pressure therapy is typically more appropriate for minor wounds and can have a number of physical adverse effects that could impede the healing process [67, 68].Using wound dressings isanother therapeutic approach for wound healing. They help the injured tissue's structural and functional recovery and may also offer defense against external pathogens. A few important points Biocompatibility, fluid (super)absorption, oxygen and water partial permeability, nonimmunogenicity, and easy, nontraumatic removal are all factors that need to be taken into account for a successful wound dressing [69, 70]. The current trend in wound care management, despite the large range of commercially available dressings, is to produce customized and performance-enhanced dressings that offer appropriatecompositional, structural, and biofunctional properties for a proper wound healing process [71, 72].

Stabilized with AgNPs functionalized with juglone, highly ordered collagen scaffolds were assessed as beneficial substrates for intercellular adhesion and cell adhesion.Alginate and nanocrystalline cellulose scaffolds thathave been combined with nanosilver to create extremely elastic, absorbent macroporous scaffolds with significant antibacterial benefits for use in wound treatment [73]. AgNPs-impregnated BC/polydopamine scaffolds were suggested as a treatment for burn injuries; the resulting nanostructured scaffolds demonstrated notable antiproteolytic and proangiogenic properties, leading to accelerated and improved wound healing [74].

Bergonzi et al. recently proposed 3D-printed plete healing Being evidenced after 25 days. The nanocomposites facilitated necrotic tissue clearance, promoted Collagen deposition and epidermis neoformation. The scaffolds also determined increased/decreased Levels of anti-inflammatory/pro- inflammatory interleukins, respectively, and upregulation of growth Factor genes involved in wound healing [75] Highly antimicrobial electrospun PLA scaffolds Modified with nanosilver and cellulose nanofibrils promoted the proliferation and normal growth Of ocular epithelial cells, with no proinflammatory reaction. The hydrophilic scaffolds were recently Proposed aseffective ocular bandages . AgNPs and lavender oil-induced synergistic antibacterial Effects when incorporated within polyurethane (PU) nanofibrous scaffolds. The resulted hydrophilic Nanocomposites encouraged improved proliferation and normal development of fibroblasts [76]

4.6. Tissue Engineering

Human tissues are made up of extremely ordered cells with distinct roles and an extracellular matrix (ECM, protein-based environment) that surrounds them at the microstructural level. containing glycosaminoglycans, which control intercellular communication, adjust cell physiology, and give three-dimensional support for cellularadhesion and proliferation. In general, acute or chronic traumas, severe inflammatory illnesses, hereditary disorders, degenerative conditions, and malignancies can all resultin the structural and functional degradation of human tissue. Healthcare professionals and scientists turned to tissue engineering's impressive potential in an attempt to overcome the limitations of organ transplantation, which included reduced bioavailability in the case of autografts and isografts, immunogenicity and graft rejection in the case of allografts and xenografts.

As a part of regenerative medicine, the desideratum of tissue engineering (TE) is represented By the fabrication of nonviable complex biocompatible systems that are able to revive the structural Integrity and functionality of damaged tissues by restoring,replacing or regenerate them [77]. Nanostructured biomaterials represent a suitable choice for TE applications, not only because they Properly interact with living systemsand possess specific and selective therapeutic purpose, but also Because they possess versatile and tunable characteristics which enable the achievement of particular Requirements, such as (i) biocompatibility (a complex feature that relies on the bidirectional interactions between nanomaterials and host cells or tissues); (ii) physicochemical properties (microstructure, Phase transitions, porosity, wettability, morphology, topography, composition, stability, reactivity); and (iii) circumstantial bioactivity [78, 79].

Given their reduced toxic effects in healthy cells, facile surface functionalization and excellent Antimicrobial activity, the impact of nanosilver-based biomaterials for TE was thoroughly evaluated. To begin with, AgNPs-embedded coatings were reported toboost the biological performances of Bioinert materials used in orthopedics and orthodontics. The simple modification of titanium Implants' surface with nanosilver resulted in significant antibacterial effects against strains Responsible for implant- associated infections while maintaining excellent biocompatibility [80 -82]

5. Conclusions

Numerous physicochemical parameters, including size, shape, concentration, surface charge, and colloidal state, have been linked to the intrinsic antimicrobial effects exhibited by silver nanoparticles (AgNPs). Additionally, the impressive available surface of AgNPs allows the coordination of numerous ligands, opening up enormous possibilities with regard to the surface functionalization of AgNPs. AgNP-based nanosystems and nanomaterials are suitable alternatives for drug delivery, wound dressing, tissue scaffold, and protective coating applications.

Numerous studies have demonstrated the advantageous benefits of AgNPs in innovative biocompatible and nanostructured materials and gadgets created for contemporary medicinal approaches.

AgNPs have additional mechanical, optical, chemical, and biological characteristics that make them desirable for the development, acquisition, testing, and clinical evaluation of performance-enhanced biomaterials and medical devices in addition to their appealing and adaptable antibacterial potential. Nevertheless, in-depth research is needed to determine their toxicity over the short and long terms as well as the processes underlying these effects.

The remarkable potential of silver nanoparticles in biomedical applications is outlined by the current constraints associated with traditional healthcare practice and the most recent difficulties brought about by nanosilver-based technology. AgNPs are excellent candidates for reaching the very close modern biomedicine desired outcome, whether we take into account the creation of new nanostructured biomaterials and devices or the modification of existing ones.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] P.H.C. Camargo, K.G. Satyanarayana, F. Wypych Nanocomposites: Synthesis, Structure, Properties And New Application Opportunities Mater Res, 12 (2009), Pp. 1-3

[2] P.H.C. Taniguchi Non the basic concept Nano-Technology Proc.Intl.Conf.Prod.Eng.Tokyo,Part II .Japan society of precision Engineering ;1974

[3] Rafique M, Sadaf I, Rafique MS, et al. A review on green synthesis of silver nanoparticles and their applications. Arif Cells Nano med Biotechnology. 2016; 45:1–20.

[4] Yin, I.X.; Zhang, J.; Zhao, I.S.; Mei, M.L.; Li, Q.; Chu, C.H. The Antibacterial Mechanism of Silver Nanoparticles and Its Application in Dentistry. Int. J. Nano med. 2020, 15, 2555–2562. [Google Scholar] [Cross Ref] [PubMed] [Green Version]

[5] Samuel, M.S.; Jose, S.; Selvaraj an, E.; Mathimani, T.; Pugazhendhi, A. Biosynthesized silver nanoparticles using Bacillus amyloliquefaciens application for cytotoxicity effect on A549 cell line and photocatalytic degradation of p-nitrophenol. J. Photo Chem. Photobiol. 2020, 202, 111642. [Google Scholar] [CrossRef] [PubMed]

[6] Albrecht, M.A.; Evans, C. W.; Raston, C. L. Green Chem. 2006, 8, 417. DOI: 10.1039/B517131H .

[7] Achmad, S.; Salmiati; Razman, S.M.; Ahmad, B.H.K.; Tony, H.; Hadi, N. A review of silver nanoparticles:Research trends, global consumption, synthesis, properties, and future challenges.J. Chin. Chem. Soc.2017, 64, 732–756.

[8] Dondi R, Su W, Griffith GA, Clark G, Burley GA (2012) Highly size-and shape- controlled synthesis of silver nanoparticles via a templated tollens reaction. Small 8(5):770–776.

[9] Azonano, xxxxhttp://www.azonano.com/Details.asp?ArticleID=1695(accessed 19.11.08)

[10] Mellati A (2014). A biodegradable thermosensitive hydrogel with tuneable properties for mimicking three-dimensional microenvironments of stem cells. RSC Advance, 4:63951-63961.

[11] Iravani, S., Korbekandi, H., Mirmohammadi, S. V. & Zolfaghari, B. Synthesis of silver nanoparticles: Chemical, physical andbiological methods. Res. Pharm. Sci. 9(6), 385–406 (2014).

[12] Ijaz, I., Gilani, E., Nazir, A. & Bukhari, A. Detail review on chemical, physical and green synthesis, classifcation, characterizations and applications of nanoparticles. Green Chem. Lett. Rev. 13(3), 59–81 (2020).

[13] Alnehia, A. et al. Phyto-mediated synthesis of silver-doped zinc oxide nanoparticles from Plectranthus barbatus leaf extract: Optical, morphological, and antibacterial properties. Biomass Convers. Biorefnery https://doi.org/10.1007/s13399-023-03907-5 (2023).

[14] Alnehia, A. et al. Structural, optical, and bioactivity properties of silver-doped zinc sulfde nanoparticles synthesized using Plec-tranthus barbatus leaf extract. J. Chem. 2023, 1–10 (2023).

[15] Elsupikhe, R.F.; Shameli, K.; Ahmad, M.B.; Ibrahim, N.A.; Zainudin, N. Green sonochemical synthesis of Silver nanoparticles at varying concentrations of κ-carrageenan. Nanoscale Res. Lett. 2015, 10, 302. [CrossRef] [PubMed]

[16] Shameli, K.; Ahmad, M.B.; Yunus, W.M.Z.W.; Ibrahim, N.A.; Gharayebi, Y.; Sedaghat, S. Synthesis of Silver/montmorillonite nanocomposites using γ-irradiation. Int. J. Nanomed. 2010, 5, 1067–1077. [CrossRef] [PubMed]

[17] Shameli, K.; Ahmad, M.B.; Yunus, W.M.; Rustaiyan, A.; Ibrahim, N.A.; Zargar, M.; Abdollahi, Y. Green Synthesis of silver/montmorillonite/chitosan bionanocomposites using the UV irradiation method and Evaluation of antibacterial activity. Int. J. Nanomed. 2010, 5, 875– 887. [CrossRef] [PubMed]

[18] Tsuji, M.; Hashimoto, M.; Nishizawa, Y.; Kubokawa, M.; Tsuji, T. Microwave- assisted synthesis of metallic Nanostructures in solution. Chem. Eur. J. 2005, 11, 440–452. [CrossRef] [PubMed]

[19] Abou El-Nour, K.M.; Eftaiha, A.; Al-Warthan, A.; Ammar, R.A. Synthesis and applications of silver Nanoparticles. Arab. J. Chem. 2010, 3, 135–140. [CrossRef]

[20] Tao, A.; Sinsermsuksakul, P.; Yang, P. Polyhedral silver nanocrystals with distinct scattering signatures Angew. Chem. Int. Ed. 2006, 45, 4597–4601. [CrossRef] [PubMed]

[21] Wiley, B.; Sun, Y.; Mayers, B.; Xia, Y. Shape-controlled synthesis of metal nanostructures: The case of silver.Chemistry 2005, 11, 454–463. [CrossRef] [PubMed]

[22] Zhang W, Qiao X, Chen J. Synthesis of silver nanoparticles—efects of Concerned parameters in water/oil microemulsion. Mater Sci Eng B. 2007;142:1–15.

[23] Wei, L.; Lu, J.; Xu, H.; Patel, A.; Chen, Z.-S.; Chen, G. Silver nanoparticles: Synthesis, properties, and Therapeutic applications. Drug. Discov. Today. 2015, 20,595–601. [CrossRef]

[24] Burdus,el, A.-C.; Gherasim, O.; Grumezescu, A.M.; Mogoantă, L.; Ficai, A.; Andronescu, E. Biomedical Applications of silver nanoparticles: An up-to-date overview. Nanomaterials 2018, 8, 681. [CrossRef]

[25] Chugh, H.; Sood, D.; Chandra, I.; Tomar, V.; Dhawan, G.; Chandra, R. Role of gold and silver nanoparticles In cancer nano-medicine. Artif. Cell. Nanomed. Biotechnol. 2018, 46, 1210– 1220. [CrossRef]

[26] G. Sergeev, T. Shabatina Colloids Surf. A: Physicochem. Eng. Aspects, 313 (2008), p. 112.

[27] J. Tate, J. A. Rogers, C. D. W. Jones, B. Vyas, D. W. Murphy, W. J. Li, Z. A. Bao, R. E. Slusher, A. Dodabalapur and H. E. Katz, Langmuir, 2000, 16, 6054–6060 CrossRef CAS.

[28] Noginov, M.A., Zhu, G., Bahoura, M., et al., 2007. The effect of gain and absorption On surface plasmos in metal nanoparticles. Appl. Phys. 86, 455–460.

[29] Ajitha B, Reddy YAK, Reddy PS (2015) Green synthesis and characterization of silver nanoparticles using Lantanacamara leaf extract. Mater Sci Eng C 49:373–381.

[30] Johnston HJ, et al. A review of the in vivo and in vitro toxicity of silver and gold particulates: particle attributes and biological mechanisms responsible for the observed toxicity. Crit Rev Toxicol. 2010;40:328–346.

[31] L.C. Stoehr, E. Gonzalez, A. Stampfl, E. Casals, A. Duschl, V. Puntes, et al.Shape matters: effects of silver nanospheres and wires on human alveolar epithelial cells Part Fibre Toxicol

[32] Ahmed S, Saifullah, Ahmad M, Swami BL, Ikram S. Green synthesis of silver nanoparticles using Azadirachta indica aqueous leaf extract. Journal of Radiation Research and Applied Science. 2016;9:1-7

[33] Kaegi, R. · Sinnet, B. · Zuleeg, S Release of silver nanoparticles from outdoor facadesEnviron. Pollut. 2010; 158:2900-2905

[34] Parisi, C. · Vigani, M. · Rodríguez-Cerezo, E.Agricultural nanotechnologies: what are the current possibilities?Nano Today. 2015; 10:124-127

[35] Qureshi AT. Silver nanoparticles as drug delivery systems [thesis]. Louisiana State University; 2013

[36] NeubertRH. Potentials of new nanocarriers for dermal and transdermal drug delivery. Eur j Pharm Biopharm. 2011;77(1):1–2. doi:10.1016/j.ejpb.2010.11.00321111043 PubMed Web of Science ®Google Scholar

[37] PatzeltA, MakWC, JungS, et al. Do nanoparticles have a future in dermal drug delivery? J Controlled Release. 2017;246:174–182. doi:10.1016/j.jconrel.2016.09.015 PubMed Web of Science ®Google Scholar

[38] FangC-L, AljuffaliIA, LiY-C, FangJ-Y. Delivery and targeting of nanoparticles into hair follicles. Ther Deliv. 2014;5(9):991–1006. doi:10.4155/tde.14.6125375342

[39] PaudelKS, MilewskiM, SwadleyCL, BrogdenNK, GhoshP, StinchcombAL. Challenges and opportunities in dermal/transdermal delivery. Ther Deliv. 2010;1(1):109–131. doi:10.4155/tde.10.1621132122

[40] GiannosSA. Identifying present challenges to reliable future transdermal drug delivery products. Ther Deliv. 2015;6(8):1033–1041. doi:10.4155/tde.15.6226419262

[41] LovelynC, AttamaAA. Current state of nanoemulsions in drug delivery. J Biomater Nanobiotechnol. 2011;2(05):626. doi:10.4236/jbnb.2011.225075

[42] AbdE, NamjoshiS, MohammedYH, RobertsMS, GriceJE. Synergistic skin penetration enhancer and nanoemulsion formulations promote the human epidermal permeation of caffeine and naproxen. J Pharm Sci. 2015.

[43] GarcêsA, AmaralM, LoboJS, SilvaA. Formulations based on solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for cutaneous use: A review. Eur J Pharm Sci. 2017.

[44] AroraR, KatiyarSS, KushwahV, JainS. Solid lipid nanoparticles and nanostructured lipid carrier-based nanotherapeutics in treatment of psoriasis: a comparative study. Expert Opin Drug Deliv. 2017;14(2):165–177. doi:10.1080/17425247.2017.126438627882780

[45] SchwarzJC, BaisaengN, HoppelM, LöwM, KeckCM, ValentaC. Ultra-small NLC for improved dermal delivery of coenzyme Q10. Int J Pharm. 2013;447(12):213–217. doi:10.1016/j.ijpharm.2013.02.03723438979

[46] El MaghrabyGM, WilliamsAC, BarryBW. Can drug-bearing liposomes penetrate intact skin? J Pharmacy Pharmacol. 2006;58(4):415–429. doi:10.1211/jpp.58.4.0001

[47] ShahSM, AshtikarM, JainAS, et al. LeciPlex, invasomes, and liposomes: a skin penetration study. Int J Pharm. 2015;490(12):391–403. doi:10.1016/j.ijpharm. 2015.05.04226002568

[48] NeubertRH. Potentials of new nanocarriers for dermal and transdermal drug delivery. Eur j Pharm Biopharm. 2011;77(1):1–2. doi:10.1016/j.ejpb. 2010.11.00321111043

[49] EidRK, EssaEA, El MaghrabyGM. Essential oils in niosomes for enhanced transdermal delivery of felodipine. Pharm Dev Technol. 2018;1–9.28347192

[50] DögeN, HönzkeS, SchumacherF, et al. Ethyl cellulose nanocarriers and nanocrystals differentially deliver dexamethasone into intact, tape-stripped or sodium lauryl sulfate- exposed ex vivo human skin-assessment by intradermal microdialysis and extraction from the different skin layers. J Controlled Release. 2016;242:25–34. doi:10.1016/j.jconrel.2016.07.009

[51] Bapat, R.A.; Chaubal, T.V.; Joshi, C.P.; Bapat, P.R.; Choudhury, H.; Pandey, M.; Gorain, B.; Kesharwani, P.An overview of application of silver nanoparticles for biomaterials in dentistry.Mater. Sci. Eng. C 2018, 91, 881–898.

[52] Lara HH, Ayala-Núnez NV, Turrent LdCI, Padilla CR. Bactericidal effect of silver nanoparticles against multidrug-Resistant bacteria. World J Microbiol Biotechnol. 2010; 26(4): 615-621.

[53] Knetsch ML, Koole LH. New strategies in the development Of antimicrobial coatings: the example of increasing usage Of silver and silver nanoparticles. Polymers. 2011; 3(1): 340-366.

[54] Pelgrift RY, Friedman AJ. Nanotechnology as a therapeutic Tool to combat microbial resistance. Adv Drug Deliv Rev. 2013; 65(13): 1803-1815.

[55] Acharya, D.; Singha, K.M.; Pandey, P.; Mohanta, B.; Rajkumari, J.; Singha, L.P. Shape dependent physical Mutilation and lethal effects of silver nanoparticles on bacteria. Sci. Rep. 2018, 8, 201. [CrossRef]

[56] Jinu, U.; Rajakumaran, S.; Senthil-Nathan, S.; Geetha, N.; Venkatachalam, P. Potential larvicidal activity of silver nanohybrids synthesized using leaf extracts of Clianthus collinus (Roxb.) Benth. ex Hook.f. and Strychnos nux-vomica L. nux-vomica against dengue, Chikungunya and Zika vectors. Physiol. Mol. Plant Pathol. 2018, 101, 163–171.

[57] Salleh, A.; Naomi, R.; Utami, N.D.; Mohammad, A.W.; Mahmoudi, E.; Mustafa, N.; Fauzi, M.B. The Potentia of Silver Nanoparticles for Antiviral and Antibacterial Applications: A Mechanism of Action. Nanomaterials 2020, 10, 1566.

[58] Mandal RP, Mandal G, Sarkar S, Bhattacharyya A, De S. "Theranostic" role of bile salt- capped silver nanoparticles - gall stone/pigment stone disruption and anticancer activity. J Photochem Photobiol B. 2017; 175: 269-281.

[59] Thakkar KN, Mhatre SS, Parikh RY. Biological synthesis of metallic nanoparticles. Nanomedicinee 2010; 6: 257-262.

[60] Parikh RY, Singh S, Prasad BLV, Patole MS, Sastry M, Schouche YS. Extracellular synthesis of crystalline silver nanoparticles and molecular evidence of silver resistance from Morganella sp.: towards understanding biochemical synthesis mechanism. ChemBioChem 2008; 9: 1415-1422

[61] Velnar, T.; Gradisnik, L. Tissue Augmentation in Wound Healing: The Role of Endothelial and Epithelial Cells. Med. Arch. 2018, 72, 444–448. [CrossRef] 348. Negut, I.; Grumezescu, V.; Grumezescu, A.M. Treatment Strategies for Infected Wounds. Molecules 2018, 23, 2392. [CrossRef]

[62] Velnar, T.; Bailey, T.; Smrkolj, V. The Wound Healing Process: An Overview of the Cellular and Molecular Mechanisms. J. Int. Med. Res. 2009, 37, 1528–1542. [CrossRef]

[63] Rodrigues, M.; Kosaric, N.; Bonham, C.A.; Gurtner, G.C. Wound Healing: A cellular perspective. Physiol. Rev. 2018, 99, 665–706. [CrossRef]

[64] Atiyeh, B.S.; Costagliola, M. Cultured epithelial autograft (CEA) in burn treatment: Three decades later. Burns 2007, 33, 405–413. [CrossRef]

[65] Diegidio, P.; Hermiz, S.J.; Ortiz-Pujols, S.; Jones, S.W.; van Duin, D.; Weber, D.J.; Cairns, B.A.; Hultman, C.S. Even Better Than the Real Thing? Xenografting in Pediatric Patients with Scald Injury. Clin. Plast. Surg. 2017, 44, 651–656. [CrossRef] [PubMed]

[66] Eggleton, P.; Bishop, A.; Smerdon, G. Safetyand efficacy of hyperbaric oxygen therapy in chronic wound Management: Current evidence. Chronic Wound Care Manag. Res. 2015, 2, 81–93. [CrossRef]

[67] Kaufman, H.; Gurevich, M.; Tamir, E.; Keren, E.; Alexander, L.; Hayes, P. Topical oxygen therapy stimulatesHealing in difficult, chronic wounds: A tertiary centre experience. J. Wound Care 2018, 27. 426–433.

[68] Lima, R.V.K.S.; Coltro, P.S.; Farina JÚNior, J.A. Negative pressure therapy for the treatment of complex Wounds. Rev. Colégio Bras. Cir. 2017, 44, 81–93. [CrossRef]

[69] Sexton, F.; Healy, D.; Keelan, S.; Alazzawi, M.; Naughton, P. A systematic review and meta-analysis comparing .The effectiveness of negative-pressure wound therapy to standard therapy in the prevention of complications After vascular surgery. Int. J. Surg. 2020, 76, 94–100. [CrossRef]

[70] Ousey, K.; Cutting, K.F.; Rogers, A.A.; Rippon, M.G. The importance of hydration in wound healing: Reinvigorating the clinical perspective. J. Wound Care 2016, 25, 124–130.

[71] Han, G.; Ceilley, R. Chronic Wound Healing: A Review of Current Management and Treatments. Adv. Ther. 2017, 34, 599–610. [CrossRef]

[72] Stoica, A.E.; Chircov, C.; Grumezescu, A.M. Nanomaterials for Wound Dressings: An Up-to-Date Overview. Molecules 2020, 25, 2699. [CrossRef]

[73] Natarajan, D.; Kiran, M.S. Fabrication of juglone functionalized silver nanoparticle stabilized collagen Scaffolds for pro-wound healing activities. Int. J. Biol. Macromol. 2019, 124, 1002–1015. [CrossRef]

[74] Bergonzi, C.; Remaggi, G.; Graiff, C.; Bergamonti, L.; Potenza, M.; Ossiprandi, M.C.; Zanotti, I.; Bernini, F.; Bettini, R.; Elviri, L. Three-Dimensional (3D) Printed Silver Nanoparticles/Alginate/Nanocrystalline Cellulose Hydrogels: Study of the Antimicrobial and Cytotoxicity Efficacy. Nanomaterials 2020, 10, 844. [CrossRef]

[75] Jiji, S.; Udhayakumar, S.; Maharajan, K.; Rose, C.; Muralidharan, C.; Kadirvelu, K. Bacterial cellulose matrix With in situ impregnation of silver nanoparticles via catecholic redox chemistry for third degree burn wound Healing. Carbohydr. Polym. 2020, 245, 116573. [CrossRef]

[76] Sofi, H.S.; Akram, T.; Tamboli, A.H.; Majeed, A.; Shabir, N.; Sheikh, F.A. Novel lavender oil and silver Nanoparticles simultaneously loaded onto polyurethane nanofibers for wound-healing applications. Int. J. Pharm. 2019, 569, 118590. [CrossRef]

[77] Zurina, I.M.; Presniakova, V.S.; Butnaru, D.V.; Svistunov, A.A.; Timashev, P.S.; Rochev,Y.A. Tissue engineering Using a combined cell sheet technology and scaffolding approach. Acta Biomater. 2020. [CrossRef]

[78] Nguyen, M.A.; Camci-Unal, G. Unconventional Tissue Engineering Materials in Disguise. Trends Biotechnol. 2020, 38, 178–190. [CrossRef]

[79] Abbasian, M.; Massoumi, B.; Mohammad-Rezaei, R.; Samadian, H.; Jaymand, M. Scaffolding polymeric Biomaterials: Are naturally occurring biological macromolecules more appropriate for tissue engineering? Int. J. Biol. Macromol. 2019, 134, 673–694. [CrossRef]

[80] Kirmanidou, Y.; Sidira, M.; Bakopoulou, A.; Tsouknidas, A.; Prymak, O.; Papi, R.; Choli- Papadopoulou, T.; Epple, M.; Michailidis, N.; Koidis, P.; et al. Assessment of cytotoxicity and antibacterial effects of silver Nanoparticle-doped titanium alloy surfaces. Dent. Mater. Off. Publ. Acad. Dent. Mater. 2019, 35, e220–e233. [CrossRef]

[81] van Hengel, I.A.J.; Putra, N.E.; Tierolf, M.; Minneboo, M.; Fluit, A.C.; Fratila- Apachitei,L.E.; Apachitei, I.; A.A. Biofunctionalization of selective laser melted porous titanium using silver and zinc Nanoparticles to prevent infections by antibiotic-resistant bacteria. Acta Biomater. 2020, 107, 325–337.[CrossRef]

[82] Odatsu, T.; Kuroshima, S.; Sato, M.; Takase, K.; Valanezhad, A.; Naito, M.; Sawase, T. Antibacterial Properties Of Nano-Ag Coating on Healing Abutment: An In Vitro and Clinical Study. Antibiotics 2020, 9, 347. [CrossRef]