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Usage areas of nanoparticles in veterinary dermatology

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ABSTRACT

Şebap Elements such as gold and silver have been used to treat various diseases since ancient times. These elements, which are used today, have been diversified and sized through research.Recently, it is seen that nanoparticles are frequently used in the medical field. Nanoparticles can be 1-1000 nanometers in size and gain biological, physical and chemical functionality due to their nano-size. The type and size of these nanoparticles are chosen according to the area in which they will be used. These prepared drugs are used for purposes such as biosensor imaging, transporting drugs to the target organ, protecting the transported substance against denaturation, increasing the immunological response, and transporting chemotherapeutic drugs. Today, with the increase in the number of dermatological cases in clinics, different treatment methods and systems are being developed. There are various nanoparticles used in dermatological cases to increase the bioavailability of topical, oral or injectable drugs and to increase the effect in the targeted area. These drugs have been used in conditions such as antimicrobial, antiparasitic, antifungal, allergen-specific immunotherapy, wound healing, tumors and atopic dermatitis. Many studies have also been carried out in the field of dermatology and it has been shown that nanoparticles used for follicular application provide advantages in dermal drug delivery, including improved skin bioavailability, increased depth of penetration, prolonged residence time, rapid transport to the skin and tissue targeting, in dermal drug delivery by using the appropriate nanoparticles in the right sizes. Particles can collect in the follicular opening and penetrate through the follicular canal when applied to the skin surface. This review has been prepared to investigate the usability of nanoparticle-derived drugs used in human medicine in veterinary applications.

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Introduction

Background: Today, Nanoparticles (NP) and nanostructured materials (NSM) represent an active research area and techno-economic sector with a full expansion in many application areas. NPS and NSMs have gained importance in technological advances due to their adjustable physicochemical properties such as melting point, wettability, electrical and thermal conductivity, catalytic activity, light absorption, and scattering. A nanometer (nm) is a unit of the International System of Units (Système international d'unités, SI), representing a length of 10-9 meters. In principle, the diameters of NSMs are usually defined as 1- to 100 nm. Today, several legislation in the European Union (EU) and the USA specifically refer to

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Nanomaterials. The use of different definitions in different jurisdictions is a major obstacle to regulatory efforts, as it creates legal hesitations in applying regulatory approaches to the same names. Therefore, there is no single internationally accepted definition for NMs (Jeevanandam et al.,2018; Karaoğlan,2017).

History of nanomaterials

More than 4500 years ago, humans benefited from the reinforcement of ceramic matrices containing natural asbestos nanofibers. Medically, gold nanoparticles have been used in various medicines from ancient times to the present day. In 2500 BC, China used nanoparticles to treat diseases. Also, many ancient cultures, such as those in India and Egypt, used gold-based medicinal preparations (Huaizhi and Yuantao, 2001). In recent years, gold nanoparticles have been used frequently as catalysts, carriers, and biosensor applications thanks to their properties (Dağlar, 2009).

Scientific terms about nanoparticles

The British Standards Institute has recently proposed definitions for scientific terms used in nanotechnology. If we give an example of definitions; Nanoscience is the science and study of matter at the nanoscale, understanding its size and structure-related properties, and comparing the emergence of individual atoms or molecules or differences in the bulk material. Nanotechnology is the manipulation and control of matter at the nanoscale using scientific knowledge of various industrial and biomedical applications. A nanomaterial is a material that has any internal or external structure at the nanoscale. A nanoparticle is a nano-sized nano-object (PAS 71:2011, Nanoparticles. Vocabulary. British Standards Institution: London, United Kingdom, 2011).

Classification of nanoparticles

Most existing NPS and NSMs can be organized into four item-based categories:

Carbon-based nanoparticles: Generally, these NMs contain carbon and exist in morphologies such as hollow tubes, ellipsoids, or spheres. Fullerenes (C60), carbon nanotubes (CNTs), carbon nanofibers, carbon black, graphene (Gr), and carbon bulbs are included in the carbon-based NM category. Laser ablation, arc discharge, and chemical vapor deposition (CVD) are important production methods in the manufacture of these carbon-based materials (excluding carbon black) (Kumar and Kumbhat, 2016).

Inorganic-based nanoparticles: These NMs include metal and metal oxide NPs and NSMs. Metals such as Au or Ag NPs can be synthesized into metal oxides such as TiO2 and ZnO NPs, and semiconductors such as silicon and ceramics (Jeevanandam et al., 2018).

3- Organic-based nanomaterials: These include NMs mostly made of organic matter, excluding carbon-based or inorganic-based NMs. The use of non-covalent (weak) interactions for the self-assembly and design of molecules helps convert organic NMs into desirable structures such as dendrimers, micelles, liposomes, and polymer NPs (Jeevanandam et al., 2018).

Composite-based nanomaterials: Composite NMs are nanoscale-sized one-phase multiphase NPs that can combine NPs with other NPs or NPs combined with larger or bulk type materials (hybrid nanofibers) and are NSMs. Composites can be any combination of carbon-based, metal-based, or organic-based NM with any form of metal, ceramic, or polymer bulk material (Jeevanandam et al., 2018).

Nanoparticle formulations

Polymeric nanoparticles: Polymeric nanoparticles are prepared by combining the active substance/drug with a polymer. The active ingredients are dissolved, held, or adsorbed onto the polymer nanoparticle surface. It also finds widespread application in veterinary medicine (Underwood and Van Eps, 2012). Studies have stated that nanoparticles carrying molecules with antigenic properties provide promising results in immunology. In veterinary medicine, nanoparticles, which are given in drinking water and released into the intestine, are used to protect animals against parasites (Alonso, 1996; Derman et al., 2013).

Solid lipid nanoparticles consist of lipids that are solid at room temperature, equilibrated with a surfactant, and suspended in an aqueous solution. The pharmaceutical is dissolved or dispersed in the lipid (Underwood and Van Eps, 2012). Solid lipid nanoparticles show several advantages over polymeric nanoparticles. For example, they have relatively higher drug retention efficacy and can be administered by multiple routes (oral, topical, and Intravenous). Moreover, hydrophobic drugs are stable in lipid matrices, protect sensitive drugs from the external environment, have minimal toxicity, and do not require the use of organic solvents in production (Mishra et al.,2010). In addition, SLNs can provide controlled-release formulations lasting up to several weeks, where they conform to mucosal surfaces, promote absorption of orally administered drugs, and are likely to cross the blood-brain barrier as they can transport drugs in the blood (Blasi et al., 2009).

Liposomes: Liposomes are highly flexible delivery systems that can transport both hydrophobic and hydrophilic substances. They can be conjugated into antibodies or ligands. They are suitable for topical, intravenous, and intramuscular use, but are rarely suitable for oral use because they are susceptible to degradation in the gastrointestinal tract. Promising

studies have been conducted on targeted drugs, imaging agents, and vaccines (Dams et al., 2000; Underwood and Eps, 2012)

Nanoemulsions consist of oil droplets dispersed in an aqueous solution. Drugs are loaded into the dispersed phase where the droplet size is typically 20-200 nm. Low-cost, solvent-free nanoemulsions have been produced for use in animal species (Vandamme and Anton, 2010), and promising results have been obtained using nanoemulsions, especially for oral and transdermal drug administration (Kang et al., 2004; Ke et al., 2005).

Micelles: Hydrophobic substances are stored in the micelle core, where they are dissolved and protected against enzymatic degradation. Micelles can be easily prepared, have low toxicity, and have the potential to be a versatile system for the effective delivery of different classes of therapeutic agents (Kim et al., 2010; Yokoyama, 2019).

Inorganic Nanoparticles have shown great potential as nanocarriers for therapeutic agents, vaccines, and imaging agents. However, their clinical use is limited by concerns of toxicity, lack of biodegradability, and permanent tissue deposition (Underwood and Eps, 2012; Fadeel and Garcia-Bennet, 2010).

Ceramic nanomaterials: Ceramic nanoparticles made of materials such as silica, alümina, and titania have several advantages over polymeric nanoparticle systems; they are easy to prepare and have the desired shape, size, and porosity, are biocompatible, and have large surface/volume ratios. In addition, they protect the absorbed particles they carry against denaturation induced by extreme pH and temperature (Underwood and Eps, 2012; Fadeel and Garcia-Bennet, 2010).

Carbon nanomaterials: Fullerenes, carbon nanotubes, and carbon nanomaterials are found and used as drug carriers. In addition, vaccines have the potential to be used as carriers because they increase the immunological response (Pantarotto et al. ,2003).

Metallic Nanomaterials: Gold, silver, and copper are the most widely used nanomaterials, most often working with gold nanoparticles (Huaizhi and Yuanto,2001; Ghosh et al., 2008). Metal nanoparticles are used in drug delivery, imaging, and cancer thermotherapy. Metal nanoparticles can be easily synthesized in various sizes (1-150 nm), are stable, and can be modified by conjugation with various functional groups (Jain et al., 2007).

Quantum dots: They are nanoparticles that are about 2-10 nm in size. The main focus is on the use of quantum dots as imaging tools in biomedical applications (Bentolila et al., 2009).

Nanotechnology & veterinary dermatology

Nanoparticle research in veterinary medicine has primarily focused on the development of therapeutic agents, vaccines, and targeting new diagnostic methods. In some of these areas, nanoparticles offer effective and scientifically validated solutions, leading to their incorporation into already marketable products (Underwood and Eps, 2012).

In many studies, nanoparticles have shown remarkable efficacy in targeting the delivery of anticancer agents, antimicrobials, analgesics, and anti-inflammatory agents (Patwekar et al., 2021).In addition to these areas of use, many studies have been carried out in the field of dermatology in recent years, and it has been concluded that nanoparticles are the future of dermal drug delivery by using appropriate nanoparticles in the right sizes (Patzelt et al. ,2016). Nanoparticles used for follicular delivery have been shown to offer some advantages over traditional routes, including improved skin bioavailability, increased depth of penetration, prolonged residence time, rapid transport to the skin, and tissue targeting (Fang et al., 2014). One of the properties that make nanoparticles interesting for topical application is their tendency to disperse and accumulate in the hair follicles. Nanoparticles have the potential to deliver drugs through follicles (Patzelt and Lademann, 2020; Mathes et al.,2016). When applied to the skin surface, particles can collect in the follicular opening and penetrate through the follicular canal. It has also been reported that nanocarriers can introduce active ingredients deep into the skin and into the systemic circulation for therapeutic purposes (Fang et al., 2014)

Nanotechnology is used for antimicrobial, antiparasitic, antifungal purposes and in allergen-specific immunotherapy (AIT), wound healing, and the treatment of skin diseases such as melanoma and atopic dermatitis.

Antimicrobial usage: The increase in antibiotic resistance among microbial pathogens has paved the way for the search for new antimicrobial techniques that will not be affected or show resistance (Wang et al., 2017). Photo-inactivation technique is one of them. Many of these photo-inactivation techniques rely on the use of various nanoparticles and nanostructures that have dimensions very similar to the wavelength of light. In a study conducted on captive penguins, lesions treated with photoinactivation or antibiotics in Bumblefoot disease, one of the most important clinical complications, were compared. There was a significant difference in the recovery rate and mean recovery time between the photoinactivation and antibiotic

groups (Nascimento et al., 2015).

In a study on mice, silver-chitosan acetate or non-silver chitosan acetate bandages were applied to infected burns after bacteria were applied to the burned areas. In conclusion, it has been shown that combining chitosan acetate with nanoparticle silver has a significant synergistic effect and that silver-chitosan acetate on bandages can treat P. aeruginosa burn infection in mice (Huang et al., 2011).

Antiparasitic-acaricide usage: Recently, metal, metal oxide, and carbon nanoparticles are highly effective against a wide variety of arthropod insects and vectors. In the study on the toxicity of nanoparticles against tick vectors of medical and veterinary importance, it was emphasized that nanoparticles are effective, but research should be expanded (Benelli et al., 2017).

Solid lipid nanoparticles (SLNs) were used for transdermal ivermectin (IVM) delivery to prevent the potential systemic toxicity of ivermectin, thus providing prolonged release without blast release. It has been shown that it can be considered an effective carrier for (Guo et al. ,2018).

Antifungal usage: In a human and dog scraping study, Malassezia was isolated and silver synthesized by green synthesis using Azadirachta indica leaf extract and characterized by UV-Visible spectrophotometer, Transmission electron microscopy (TEM), X-ray diffraction spectrophotometer (XRD), and Fourier transform infrared. The antifungal activity of nanoparticles was evaluated. The characteristic silver nanoparticles inhibit the growth of Malassezia species by forming a scavenging zone. It has been reported that silver nanoparticles can be an alternative to treat fungal infections (Saranya et al., 2016).

In a study on plants, it was observed that colloidal silver inhibited the mycelium growth of various fungal species (Venat et al.,2018).

Allergen-specific immunotherapy (asit) usage: Encapsulation of allergens or DNA vaccines with nanostructures in rodents has made it possible to achieve higher local concentrations, the protein/DNA molecules can be protected from degradation, and targeted access to the site of action. It has been stated that the encapsulated allergen can be prevented from being recognized by the immune system, especially by IgE antibodies, and that agents containing nanoparticles can offer a safer and potentially more effective treatment method for allergic diseases (Pohlit et al., 2017).

Use of nanoparticles in wound healing: It has been proven by studies that gelatin-silver nanoparticles have an excellent film-forming ability that strengthens wound healing properties . Gold nanoparticles have antibacterial and biocidal properties that help prevent infection in burns, traumatic wounds, and diabetic ulcers. It has been reported to have properties (Leu et al., 2012).

In another study, faster healing was observed in treatment with silver in wound treatment trials with turmeric and silver nanoparticles in rabbits (Islam et al. ,2015).

In the treatment of melanoma usage: It has been emphasized that nanoparticles are effective in the absorption and distribution of drugs in the chemotherapy phase in melanoma and that more studies on cell targeting and distribution are needed (Naves et al., 2017).

Atopic dermatitis usage: In human medical research, nanocarriers have been investigated for atopic dermatitis, acne vulgaris, and hyperpigmented skin lesions. In the use of various nanoparticles in atopic dermatitis in humans, with the aid of versatile nanocarriers, it is possible to explore new strategies, together with new routes of administration, for the optimization of skin-specific nanoparticulate systems to treat atopic dermatitis. It has been predicted that methodologies based on nanotechnology will revolutionize aspects of clinical dermatology (Weber et al., 2018).

In a study on atopic dermatitis in dogs, the clinical and immunological effects of gelatin nanoparticle (GNP) bound CpG ODN (CpG GNP) on patients were evaluated. A significant reduction in lesions and pruritus was observed (Wagner et al., 2017).

Filling gold nanoparticles with drugs such as Ruxolitinib (jack 2 inhibitors) in the treatment of alopecia in humans has been indicated as an ideal method for triggered localized drug release to the hair follicle, and it has been observed that they can be targeted to stem cells, immune cells or various key elements in skin physiology. GNPs are hydrophobic with skin lipids. It has been stated that it interacts and causes the deterioration of lipids, and as a result, it contributes to the increase of skin porosity and permeability to drugs (Boca et al., 2017).

Conclusion

It has been concluded that in addition to the studies in veterinary medicine, studies in human medicine can be adapted to veterinary medicine, and the use of nanoparticles in veterinary dermatology can be increased with new and larger studies and can be used as an alternative method in the treatment of dermatological diseases.

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