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NANOPARTICLES USED AS A NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

A significant amount of research has been conducted in the last few years based on novel drug delivery systems, which use particulate vesicle systems as such drug carriers for both small and large molecules. Drug carriers in vesicle drug delivery systems include liposomes, nanoparticles, microspheres, niosomes, pronisomes, ethosomes and proliposomes. Nanoparticles are important to commerce, eight different types of particles will be examined orderly to evaluate the effects of size, shape, and composition on skin toxicity, absorption, and distribution. To create nanoparticles, a variety of polymers have been employed. Drugs' therapeutic effects have been enhanced and their negative effects have been reduced thanks to nanoparticles. A wide range of substances, including proteins, polysaccharides, and synthetic polymers, can be used to create nanoparticles. The three most common ways to create nanoparticles are dispersing preformed polymers; polymerizing monomers; and ionic gelation or coacervation of hydrophilic polymers. Evaluation of Nanoparticles is based on drug entrapment efficiency, particle shape, partical size and zeta potential. The impact of nanoparticles' interactions with the body depends on their size, chemical composition, surface structure, solubility, shape. Nanoparticles are applied in tumor targeting using nanoparticulate delivery system, gene therapy, cell repair and antimicrobial activity. Types of nanoparticals are liposomes magnetic dentrimars, nanogels, micells etc. there are huge future prospects of nanoparticals in medicinal approaches.

KEYWORDS: Nanoparticles, polymerization, dispersion, liposomes, coacervation, nanomedicines.

INTRODUCTION[1-4]

Particulate dispersions or solid particles with a size range of 10–1000 nm are referred as nanoparticles. The medication was encapsulated, dissolved, or linked to a matrix of nanoparticles. One can obtain nanoparticles, nanospheres, or nanocapsules depending on the preparation technique used. Whereas nanospheres are matrix systems where the drug is uniformly and physically spread, nanocapsules are systems where the drug is contained within a hollow surrounded by a special polymer membrane. Recently, biodegradable polymeric nanoparticles are known as long-circulating particles which are coated with hydrophilic polymers like polyethylene glycol (PEG) have been explored as possible drug delivery vehicles due to their capacity to circulate for an extended amount of time, target a specific organ, and function as carriers of DNA in genes.

The fundamentals of illness diagnosis, treatment, and prevention are starting to shift as a result of the development of a broad range of nanoscale technologies. The National Institutes of Health refers to these technical advancements as "nanomedicines" because they have the capacity to transform molecular findings from proteomics and genomics into broad benefits for patients. Nanomedicines is a broad field that includes functionalized carbon nanotubes as nanoparticles, "nano mechanics" (such as those made from replaceable DNA parts and DNA scaffolds like octahedron and stick cube), shape memory polymers as molecular switches, nonporous membranes, nanofibers and polymeric nano constructs as biomaterials (e.g., molecular self-assembly and nano-fibres of peptides and peptide amphiphiles for tissue engineering), and nanoscale micro-fabrication based devices (e.g. silicon microchips for drug release and micro machined hollow needles and two dimensional needles assay from single crystal silicon), sensors, and laboratory diagnostics.[5]

Assessing the nature of the interaction between synthetic nanoparticles and the skin including dermal absorption, cutaneous toxicity, and the capacity to spread to the skin following systemic exposure has been the topic of numerous studies. One of the main ways that people might be exposed to toxins, including new nanoparticles, is through their skin. Nevertheless, it is unknown if systemically injected particles might collect in dermal tissue or if they are absorbed via the stratum corneum barrier. We has created a compassionate, alternative animal model that has undergone thorough validation and is a good predictor of in vivo human dermal absorption. This model is perfect for evaluating both the skin's ability to absorb nanoparticles and their capacity to accumulate in it following systemic exposure. Iron oxide,

cadmium selenide, and carbon fullerene nanoparticles all of which are representative of the wide range of nanoparticles now in use by industry will be used in these investigations. From these manufactured nanoparticles that are important to commerce, eight different types of particles will be examined in order to evaluate the effects of size, shape, and composition on skin toxicity, absorption, and distribution. These data would offer an initial but pertinent evaluation of the two crucial elements of any risk assessment cutaneous hazard following topical and systemic exposure, as well as systemic exposure following topical treatment. We hypothesize that if carbon nanoparticles are unintentionally altered or exposed before being cleaned, they may cause undesirable effects if they penetrate tissues.

As of right now, not much is known about how artificial nanoparticles interact with biological tissues. Any risk assessment must include certain basic components, such as information on exposure (such as absorption) and danger (such as toxicity). This proposal focuses on how interactions between nanoparticles and the skin affect health.

In addition to producing data on the potential toxicity of nanoparticles to keratinocytes, this integrated research program will evaluate the ability of nanoparticles to either absorb into skin following topical exposure or distribute into skin following systemic exposure via an alternative mode of administration. The limits of a dermal risk assessment for exposure to produced nanoparticles will be revealed at the end of the study.[6]

Preparation of nanoparticles[8]

A wide range of substances, including proteins, polysaccharides, and synthetic polymers, can be used to create nanoparticles. The required size of the nanoparticle, the drug's intrinsic qualities (such as stability and aqueous solubility), the surface features (such as charge and permeability), the desired drug release profile, the degree of biodegradability, biocompatibility, and toxicity, and the antigenicity of the finished product all play a role in the selection of matrix materials. The three most common ways to create nanoparticles are: (1) dispersing preformed polymers; (2) polymerizing monomers; and (3) ionic gelation or coacervation of hydrophilic polymers.

Dispersion of preformed polymers[9,10]

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Solvent evaporation method[11]

This procedure involves dissolving the polymer in an organic solvent, such as ethyl acetate, dichloromethane, or chloroform, which is also used to dissolve the hydrophobic medication. To create an oil in water (o/w) emulsion, the polymer and drug solution mixture is subsequently emulsified in an aqueous solution including a surfactant or emulsifying agents. Either by lowering pressure or by constantly stirring, the organic solvent is removed after a stable emulsion has formed. It was discovered that the kind and concentration of stabilizer, homogenizer speed, and polymer concentration all affected particle size. Often, ultrasonication or high-speed homogenization are used to achieve tiny particle sizes.

Polymerization method[12,13,14]

Using this technique, monomers are polymerized in an aqueous solution to create nanoparticles. The drug is included into the polymerization process by either dissolving in the polymerization liquid or adhering to the nanoparticles once polymerization is finished. By using ultracentrifugation and re-suspending the particles in an isotonic surfactant-free solution, the nanoparticle suspension is further filtered to exclude different stabilizers and surfactants used for polymerization. It has been claimed that this method can be used to create polyalkylcyanoacrylate or polybutylcyanoacrylate nanoparticles.

Coacervation or ionic gelation method[15]

The process of creating nanoparticles with hydrophilic polymers that degrade naturally, like sodium alginate, chitosan, and gelatin. Ionic gelation is a technique that Calvo and colleagues devised to produce hydrophilic chitosan nanoparticles. Through this process, the positively charged amino group of chitosan combines with the negatively charged tripolyphosphate to generate nanometer sized coacervates**.**

Evaluation of nanoparticles

$$\text{Drug Entrapment Efficiency (\%)} = \frac{\text{Amount of released from the lysed nanoparticle}}{\text{Amount of drug Initially taken to prepare the nanoparticles}} \text{X100}$$

The nanoparticles were separated from the aqueous medium by ultracentrifugation at 10,000 rpm for 30 min at 5 c. Then the resulting supernatant solution was decanted and dispersed into phosphate buffer saline pH 7.4. Thus the procedure was repeated twice to remove the unentrapped drug molecules completely. The amount of drug entrapped in the nanoparticles was determined as the difference between the total amount of drug used to prepare the nanoparticles and the amount of drug present in the aqueous medium.

Particle Shape[17]

Nanoparticles possess a variety of shapes and their names are characterized by their different shapes.

For example, there are nanospheres that are spherical, nanoreefs, nanoboxes, nanoclusters, nanotubes etc. These shapes or morphologies sometimes arise spontaneously as an effect of a templating or directing agent during synthesis for example during miscellar emulsions or anodized alumina pores, or from the innate crystallographic growth patterns of the materials themselves.

Particle size[18]

The most crucial aspects of nanoparticle systems are the size and distribution of the particles. They ascertain the nanoparticle system's in vivo distribution, biological destiny, toxicity, and targeting capacity.

Furthermore, they have the ability to affect the stability, drug loading, and drug release of nanoparticles. Particle size can currently be determined more quickly and often using dynamic light scattering or photon-correlation spectroscopy. Scanning or transmission electron microscopy is typically used to validate the results of photon- correlation spectroscopy (SEM or TEM).

Zeta potential[19]

A typical method for characterizing a nanoparticle's surface charge property is to use its zeta potential. It is impacted by the makeup of the particle as well as the medium in which it is

distributed, and it represents the electrical potential of particles. It has been demonstrated that nanoparticles having a zeta potential greater than (±) 30 mV remain stable in suspension because the surface charge keeps the particles from aggregating.

Nanoparticle Properties and Safety[20,21]

The toxicity of nanoparticles research suggests that some of these products may enter the human body and become toxic at the cellular level in the tissues and organs. The impact of nanoparticles' interactions with the body depends on their size, chemical composition, surface structure, solubility, shape, and the way that individual particles accumulate together. Because of their small size and higher specific surface area, they can readily bind with transport toxic pollutants, which when inhaled can cause a variety of pulmonary diseases in mammals. Inhaled nanoparticles can translate throughout the body to the extent that they penetrate it. They can freely circulate through the blood and arrive at organs such as the liver or brain. It may pass across the blood-brain barrier and enter the lungs more deeply. It is possible for skin contact to occur when handling the nanoparticles. Due to its electron-attracting properties, fullerense and bucky balls produce harmful free radicals. Studies on the toxicity of nanoparticles and carbon-based compounds have been carried out. According to published research, ultrafine particles with little solubility have a higher mass-to-mass toxicity than bigger particles.

Applications of Nanoparticles

Tumor targeting using Nanoparticulate delivery system[22]

The justification for employing nanoparticles for tumor targeting is based on the following:

(1) Active nanoparticles improved permeability and retention effect will enable the delivery of a concentrated dosage of medication in the region of the tumor targets.

(2) By limiting medication distribution to the target organ, nanoparticles will lower the amount of drugs that are exposed to healthy tissues. In comparison to mice treated with free doxorubicin, Verdun. showed that mice treated with doxorubicin embedded into poly (isohexylcynoacrylate) nanospheres showed greater concentrations of doxorubicin in the liver, spleen, and lungs.

Nanoparticles for Gene delivery[23]

In order to trigger an immune response, polynucleotide vaccines transfer genes encoding pertinent antigens to host cells where they are produced. This results in the production of the antigenic protein close to expert antigen-presenting cells. Because intracellular protein

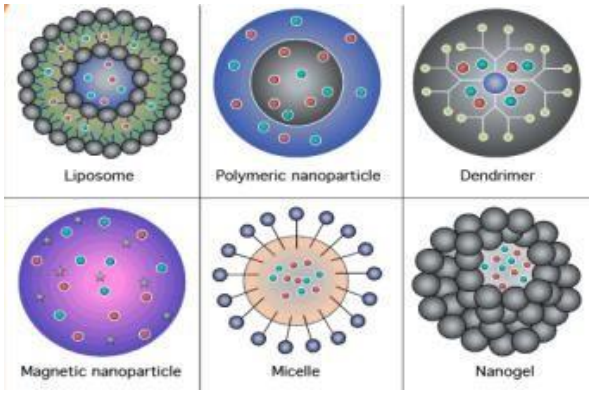
creation stimulates both arms of the immune system more than extracellular protein deposition, such vaccines result in both humoral and cell-mediated protection.

Nanotechnology in Medicine Application: Anti-Microbial Techniques[24]

The use of nanocrystalline silver as an antibacterial agent for wound therapy was among the first uses of nanomedicine. Staph infections can be prevented with a lotion containing nanoparticles. Nitric oxide gas, which is known to destroy germs, is present in the nanoparticles. Utilizing the nanoparticle cream to produce nitric oxide gas at the location of staph abscesses dramatically decreased the infection, according to studies conducted on mice.

Burn dressing with antibotic nanocapsules applied on top. The antibotics are released from the nanocapsules when an infection begins due to dangerous bacteria in the wound. This lowers the frequency of dressing changes and enables considerably faster treatment of an infection. An notion that's welcome in the early study stages is the elimination of bacterial infections in a patient within minutes, instead of delivering treatment with antibiotics over a period of weeks.

Type of nanoparticles



Liposomes

Liposomes are concentric bilayered vesicles with a membranous lipid bilayer mostly made of synthetic or natural phospholipids enclosing the entire aqueous volume. The size, surface charge, and number of bilayers of liposomes are characterized. Its many benefits, including its amphiphilic nature, biocompatibility, and simplicity of surface modification, make it a viable choice for a delivery system for biotech medications. Since their invention, liposomes have been successfully applied in the fields of biology, biochemistry, and medicine. These significantly change the loaded drug's pharmacokinetic profile, particularly for proteins and peptides, and are readily changed by attaching polyethylene glycol units (PEG) to their

surface to turn them into stealth liposomes that lengthen the drug's half-life in circulation.[25-27]

Polymeric nanoparticles

In comparison to SLN or nanosuspensions polymeric nanoparticles (PNPs) consists of a biodegradable polymer. The advantages of using PNPs in drug delivery are many, being the most important that they generally increase the stability of any volatile pharmaceutical agents and that they are easily and cheaply fabricated in large quantities by a multitude of methods. Also, polymeric nanoparticles may have engineered specificity, allowing them to deliver a higher concentration of pharmaceutical agent to a desired location.[28] Polymeric nanoparticles are a broad class comprised of both vesicular systems (nanocapsules) and matrix systems (nanospheres).

Dendrimers, a unique class of polymers, are highly branched macromolecules whose size and shape can be precisely controlled. Dendrimers are fabricated from monomers using either convergent or divergent step growth polymerization. The well-defined structure, mono dispersity of size, surface functionalization capability, and stability are properties of dendrimers that make them attractive drug carrier candidates. Drug molecules can be incorporated into dendrimers via either complexation or encapsulation. Dendrimers are being investigated for both drug and gene delivery, as carriers for penicillin, and for use in anticancer therapy.[29]

Micelle

Mixed micelles possess several basic properties desirable for a Nano drug delivery system, A hydrophilic coating around a drug-loading core which allows for solubilization of water insoluble drugs and protection of incorporated proteins or nucleic acids from their degradation at off-target sites.

Nanoparticles as drug carrier vehicle

It helps in improving solubility and bioavailability, reducing toxicity, enhancing release and providing better formulation opportunities for drugs.

Major advantages of nano-sizing includes,

1. increased surface area,
2. enhanced solubility,
3. increased rate of dissolution,

4. increased oral bioavailability,
5. more rapid onset of therapeutic action,
6. less amount of dose required,
7. decreased fed/fasted variability and
8. decreased patient-to-patient variability.

They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.

Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction; this is an important factor for preserving the drug activity. Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.

Generally, nanoparticles have relatively higher intracellular uptake compared to microparticles and are available to a much wider range of biological targets due to their small size and relative mobility. 100 nm nanoparticles had a 2.5 fold greater uptake than 1 μm microparticles, and 6 fold greater uptake than 10 μm microparticles. Nanotechnology offered numerous smart materials that are used for tissue repair and replacement, implant coatings, tissue regeneration scaffolds, structural implant materials, bone repair, bioresorbable materials, some implantable devices (sensory aids, retina implants etc.), surgical aids, operating tools, and smart instruments.

Future of nanomedicine and drug delivery system

The science of nanomedicine is currently among the most fascinating areas of research. A lot of research in this field in the last two decades has already led to the filling of 1500 patents and completion of several dozens of clinical trials.[30] As outlined in the various sections above, cancer appears to be the best example of diseases where both its diagnosis and therapy have benefitted from nonmedical technologies. By using various types of nanoparticles for the delivery of the accurate amount of drug to the affected cells such as the cancer/tumour cells, without disturbing the physiology of the normal cells, the application of nanomedicine and nano-drug delivery system is certainly the trend that will remain to be the future arena of research and development for decades to come. The examples of nanoparticles showed in this communications are not uniform in their size, with some truly measuring in nanometres while

others are measured in sub-micrometres (over 100 nm). More research on materials with more consistent uniformity and drug loading and release capacity would be the further area of research. Considerable amount of progress in the use of metals-based nanoparticles for diagnostic purposes has also been addressed in this review. Te application of these metals including gold and silver both in diagnosis and therapy is an area of research that could potentially lead to wider application of nanomedicines in the future. One major enthusiasm in this direction includes the gold- nanoparticles that appear to be well absorbed in soft tumour tissues and making the tumour susceptible to radiation (e.g., in the near infrared region) based heat therapy for selective elimination. Despite the overwhelming understanding of the future prospect of nanomedicine and nano-drug delivery system, its real impact in healthcare system, even in cancer therapy/diagnosis, remains to be very limited. This attributes to the field being a new area of science with only two decades of real research on the subject and many key fundamental attributes still being unknown. The fundamental markers of diseased tissues including key biological markers that allow absolute targeting without altering the normal cellular process is one main future area of research. Ultimately, the application of nanomedicine will advance with our increasing knowledge of diseases at molecular level or that mirrors a nanomaterial-subcellular size comparable marker identification to open up avenues.

Advantages of nanoparticles in medicine

Because they may enter cells and have specialized cell-binding properties, nanoparticles' small size is very useful in medicine. They can also circulate widely throughout the body. These characteristics have made it possible to improve imaging of tumors and other sick tissues in the body, as well as organs. Additionally, they have made it easier to create novel approaches to administering treatment, such as localized heating (hyperthermia), obstructing the blood supply to malignant growths, or transporting medication payloads.

Radioactive technetium has been replaced by magnetic nanoparticles to trace the progression of cancer along lymph nodes. The way the nanoparticles function is by taking advantage of the shift in contrast caused by minute amounts of superparamagnetic iron oxide in magnetic resonance. By causing them to heat up and locally destroy tissue due to an alternating magnetic field, these particles can also be employed to eliminate tumors by causing hyperthermia.

Nanoparticles can be engineered to improve ultrasound or positron emission tomography (PET) images, as well as fluorescence imaging. These techniques usually necessitate that the nanoparticle possess the ability to identify a certain cell type or stage of illness. Theoretically, the concept of targeting could also help with the targeted delivery of a medication to a specific illness site. The medication may be delivered via liposomes or nanocapsules, or it may be delivered in the form of a porous nanosponge structure that is subsequently bound by bonds at the intended location to enable a gradual release of the medication.

Nanoparticles and nanofibres play an important part in the design and manufacture of novel scaffold structures for tissue and bone repair. The nanomaterials used in such scaffolds are biocompatible. For example, nanoparticles of calcium hydroxyapatite, a natural component of bone, used in combination with collagen or collagen substitutes could be used in future tissue-repair therapies.[31]

CONCLUSION

Nanoparticulate systems have great potentials, being able to convert poorly soluble, poorly absorbed and labile biological active substance into promising deliverable drugs. Generally, nanoparticle have relatively higher intracellular uptake compared to microparticles and available to a wide range of biological targets due to their small size and relative mobility.

The present review discusses the recent advances in nanomedicines, including technological progresses in the delivery of old and new drugs as well as novel diagnostic methodologies. A range of nano dimensional materials, including nanorobots and nano sensors that are applicable to diagnose, precisely deliver to targets, sense or activate materials in live system have been outlined. Initially, the use of nanotechnology was largely based on enhancing the solubility, absorption, bioavailability, and controlled-release of drugs. Even though the discovery of nanodrugs deal with high levels of uncertainties, and the discovery of pharmacologically active compounds from natural sources is not a favoured option today, as compared to some 50 years ago; hence enhancing the efficacy of known natural bioactive compounds through nanotechnology has become a common feature. Good examples are the therapeutic application of nanotechnology for berberine, curcumin, ellagic acid, resveratrol, curcumin and quercetin. Te efcacy of these natural products has greatly improved through the use of nanocarriers formulated with gold, silver, cadmium sulphide, and titanium dioxide polymeric nanoparticles together with solid lipid nanoparticles, crystal nanoparticles, liposomes, micelles, superparamagnetic iron oxide nanoparticles and dendrimers. Tere has

been a continued demand for novel natural biomaterials for their quality of being biodegradable, biocompatible, readily availability, renewable and low toxicity. Beyond identifying such polysaccharides and proteins natural biopolymers, research on making them more stable under industrial processing environment and biological matrix through techniques such as crosslinking is among the most advanced research area nowadays. Polymeric nanoparticles (nanocapsules and nanospheres) synthesized through solvent evaporation, emulsion polymerization and surfactant-free emulsion polymerization have also been widely introduced. One of the great intrest in the development of nanomedicine in recent years relates to the integration of therapy and diagnosis (theranostic) as exemplifed by cancer as a disease model. Good examples have been encapsulated such as, oleic acid-coated iron oxide nanoparticles for diagnostic applications through near-infrared; photodynamic detection of colorectal cancer using alginate and folic acid based chitosan nanoparticles; utilization of cathepsin B as metastatic processes fuorogenic peptide probes conjugated to glycol chitosan nanoparticles; iron oxide coated hyaluronic acid as a biopolymeric material in cancer therapy; and dextran among others. Since the 1990s, the list of FDA-approved nanotechnology-based products and clinical trials has staggeringly increased and include synthetic polymer particles; liposome formulations; micellar nanoparticles; protein nanoparticles; nanocrystals and many others often in combination with drugs or biologics. Even though regulatory mechanisms for nanomedicines along with safety/toxicity assessments will be the subject of further development in the future, nanomedicine has already revolutionized the way we discover and administer drugs in biological systems. Tanks to advances in nanomedicine, our ability to diagnose diseases and even combining diagnosis with therapy has also became a reality.

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