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Recent Application of Nanoparticles in Drug Delivery System

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Abstract

This review is mainly focused on the Nanoparticles and their applications as they are simplest form of structures with size range in the nm. Described as any gathering of atoms bonded together with a structural having the radius of less than 100 nm is considered a nanoparticle. Recently the applications of nanoparticles are wide and used in many different dosage forms due to their characteristics like good solubility, less size and better penetrability. The various methods are to be used to prepare nanoparticles such as Emulsion-Solvent Evaporation Method, Double Emulsion and Evaporation Method, Salting out Method, Emulsions Diffusion Method, Solvent Displacement or Precipitation method, Polymerization method and Coacervation or ionic gelation method. Recent advance applications of nanoparticles in micro wiring are cell specific, internalization, vaccine delivery and gene delivery etc. Nanoparticles are used in the advanced field of medication as well the cancer treatment or for the orthopedic implants. The nanoparticle reflects very high solubility as well fast penetration that makes nanoparticles used in numerous dosage forms

Keywords: *Recent applications, Nanoparticles, drug delivery systems, Vaccine delivery.*

INTRODUCTION

The word nano comes from the very old Greek νᾶνος all the way through the Latin word nanus meaning exactly dwarf and by extension, very small. Within the rule of

International System of Units (SI) that used to indicate a reduction factor of 109 times.1 Thus the nanonized world is typically measured in nanometers (1nm corresponding to 10-9 m) and it cover the systems whose size is above molecular dimensions and below macroscopic ones (it generally ranges between 1 nm and 100 nm). The nanotechnology is the science of the small and the very small where it use and manipulation of matter at a minuscule scale. On this tiny size, atoms and molecules work differently hence provide a multiplicity of surprising and exciting uses. Both nanotechnology and Nano science studies have now emerged very fast during the last few years in a wide range of product domains.2

That gives many prospects for the development of materials, including for medical applications, where conventional techniques may be not suitable. Nanotechnology can be viewed as a multiple technique that often referred to asthe 'tiny science'; nanotechnology does not simply mean tiny structures and products. The features of Nano scale are often incorporated into bulk materials and large surfaces as well. Nanotechnology symbolize the design, production and use of materials at atomic, molecular and Nano molecular scales, in order to fabricate new man-sized materials. The pharmaceutical nanoparticles are distinct as solid, submicron-sized (below 100 nm in diameter) drug carrier that may or may not be biodegradable.The word nanoparticle combined for both nanospheres and Nano capsules. Nano spheres are matrix system in which drug is uniformly dispersed, while Nano capsules are the system in which the drug is surrounded by a distinctive polymeric membrane.2,3

Objective to Develop the Nanoparticles are as, 3

- Delivery system as nanoparticles
- Control particle size
- Surface properties
- Release of pharmacologically active agents
- To achieve the site specific action of the drug
- To increase the stability of drugs

Advantages and Disadvantages of Nanoparticles 3,4

Advantages

- Ease of manipulation of the particle size and surface characteristics of nanoparticles.
- The nanoparticle surface can be modified to alter bio distribution of drugs with subsequent clearance of the

drug so as to achieve maximum therapeutic efficacy.

- Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents.
- Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction.
- Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.
- Liposomes and polymer based Nano particulates are generally biodegradable, do not accumulate in the body and so are possibly risk free.
- Small sized nanoparticles can penetrate through smaller capillaries, which could allow efficient drug accumulation at the target sites.

Disadvantages

- Altered physical properties which lead to particle – particle aggregation.
- Smaller the particles size greater the surface area and this property makes nanoparticles very reactive in the cellular environment.
- Small particles size results in limited drug loading and burst release. These practical problems have to be sorted out before nanoparticles can be used clinically.

Benefits of the Nanoparticles in Drug Delivery System

- After parenteral administration to achieve passive or active drug targeting particle size and surface characteristics of nanoparticles can be easily manipulated.
- For achieve high drug therapeutic efficacy and less side effects, during the transportation they control and sustain release of the drug & at the site of localization, altering distribution of the drug and subsequent clearance of the drug.
- Through attaching targeting ligands to surface of particles or use of magnetic guidance site-specific targeting can be achieved.
- Including the oral, intra-ocular, parenteraland nasal, the system can be used for various routes of administration.
- Surrounded by the body, drug delivery to tiny areas can be achieved better by nanoparticles.
- Engineering has enables the researchers to exercise precisely on this scale and previously control over the biomaterials and physical features of polymers. Nanoparticles those

provide efficient delivery of drug to various parts of the body by overcoming the resistance offered by the physiological barriers in the body which is directly affected by particle size.

- Nanoparticles may aid in to efficient drug delivery by improving the aqueous solubility of poorly soluble drugs and increase bioavailability for organized release of drug molecules, and in accurate drug targeting.
- For targeted drug delivery, the surface properties of nanoparticles can be altered for proteins, small molecules, peptides, and nucleic acids loaded nanoparticles are not recognized by immune system and targeted to particular tissue types efficiently.
- For targeting nano drug carriers drug toxicity can be reduced and more efficient drug distribution can be afforded.5,6

NANOPARTICLES: TYPES BASED ON THE MANUFACTURING METALS USED

Silver

These are the most effective as of their good antimicrobial efficacy against bacteria, viruses and other eukaryotic microorganisms as well. Amongst all the nanomaterial's these are most widely used as antimicrobial agents, for sunscreen lotions etc. 6

Gold

Useful in identification of protein interactions in immune-chemical studies. Gold nanoparticles are also used in DNA fingerprinting, used as lab tracer todetect existence of DNA in a sample. The aminoglycoside antibiotics i.e. streptomycin, gentamycin and neomycin are also spotted by using these nanoparticles. Even the detection can be form of cancer stem cells, diagnosis of cancer and identification of different classes of bacteria done by help of Gold nano rods. 6

Alloy

The structural properties of alloy nanoparticles are different. Where silver flakes are most commonly used due to their maximum electrical conductivity among other metal fillers, their oxides can also have relatively greater conductivity. 6

Magnetic

The magnetic nanoparticles are well known as biocompatible i.e. magnetite and magnetite. In magnetic resonance imaging (MRI), guided drug delivery, targeted cancer treatment, gene therapy, stem cell

sorting and manipulation and for DNA analysis they are actively considered.6

OTHER TYPES OF NANO PARTICLES

Polymeric Nanoparticles

These are colloidal structures composed of synthetic or semi synthetic polymers. The drug usually dissolved, entrapped, encapsulated or attached to a Nano particulate matrix. The method of preparation is as nanoparticles, Nano spheres or Nano capsule can be obtained. The Nano capsules are systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while Nano spheres are matrix systems in which the drug is physically and uniformly dispersed.7

Solid Lipid Nanoparticles

These are very new type of colloidal system of drug carrier system very suitable for intravenous administration. This system consists of spherical shaped solid lipid particles in the Nano sized range, which is dispersed in water or in surfactant solution.7

Formulation Methods of Nanoparticles

For the formulation of nanoparticles, the selection of the appropriate method is mainly depended on the drug to be loaded and physicochemical properties of the polymer. The basic preparation methods of nanoparticle are includes as below, 8

Emulsion-Solvent Evaporation Method

The nanoparticles are prepared by using these methods using two steps are mainly involved in this method. An aqueous phase used for emulsification of the polymer solution required in the first step and in the second step, evaporation of polymer solution occurs and Nano spheres are formed by inducing the polymer precipitation. The collection of nanoparticles done by ultracentrifugation method and to remove free drug or residue, then washed with distilled water and for storage these are lyophilized. This method is also called as solvent evaporation method and high pressure emulsification.8

Double Emulsion and Evaporation Method

Here aqueous drug solutions are made then added to organic polymer solution with vigorous stirring to form w/o emulsions. Through continuous stirring to form mixed emulsion (w/o/w), this w/o emulsion is further add into another aqueous phase. After that by the evaporation solvent is separated, and by using centrifugation at high speed nano particles can be isolated.

But before lyophilisation the prepared nanoparticles must be washed and then the variables used in this method are incorporated quantity of hydrophilic drug, the amount of polymer, the volume of aqueous phase and the stabilizer quantity. The of nano particles characterization can also affected by these variables.9

Salting Out Method

In salting-out from aqueous solution the water-miscible solvent is totally separated by this method. Firstly in a solvent, polymer and drug are completely dissolved which is as a result containing the salting out agent, electrolytes, such as calcium chloride and magnesium chloride or sucrose as non- electrolytes, and polyvinylpyrrolidone (PVP) or may be hydroxyethylcellulose as a colloidal stabilizer into an aqueous gel are emulsified. Now this oil in water emulsion is further diluted with water or with other aqueous phase to increase the diffusion of solvent that indicates the formation of Nano spheres in the system.9, 10

Emulsions Diffusion Method

For formulating nanoparticles, emulsions diffusion method is another method which is used very commonly. The polymer used for encapsulating is dissolved in a solvent which is partially miscible with water may be propylene carbonate, benzyl alcohol and the initial thermodynamic equilibrium of both liquids saturated with water should be ensured.10 After that the polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer, leading to solvent diffusion to the external phase and according to the oil-to- polymer ratio Nano spheres or Nano capsules are formed. At the end, according to boiling point the solvent is removed byevaporation or filtration. This technique has several advantages, such as high reproducibility (batch-to-batch), no requirement of homogenization, high encapsulation efficiencies (generally 70%), very easy as narrow size distributionand ease of scale-up.[11]

Solvent displacement/Precipitation Method

This method includes from an organic solution, the settle down of a preformed polymerand in the aqueous medium the diffusion of theorganic solvent in the presence or absence of surfactant. In semi-polar water miscible solvent such as acetone or ethanol, polymers, drug and lipophilic surfactant are dissolved. Then solution is poured or injected using the magnetic stirring, into stabilizer containing aqueous solution. In a very fast solvent diffusion nano particles are formed. Then

under reduced pressure solvent is removed from the suspension. The particles size is also affected byrate of addition of the organic phase into theaqueous phase.12

Polymerization Method

In this method, polymerization of monomers is done in an aqueous solution and after polymerization completed, drug is integrated either by adsorption onto the nanoparticles or by being dissolved in the polymerization medium. To remove various stabilizers and surfactants, employed for polymerization by ultra-centrifugation the nanoparticle suspension is then purified and into isotonic surfactant-free medium re-suspending the particles.13

Coacervationor Ionic Gelation Method

For formulation of nanoparticles much research has been focused using biodegradable hydrophilic polymers such as chitosan, sodium alginate and gelatin. This method contains twoaqueous phases, in which one is the polymer chitosan and the other phase is a polyanioni.e. Sodium tripolyphosphate in this method, interaction of positively charged amino group of chitosan with negative charged tri polyphosphate occurs which form coacervates with ananometer size range. Electrostatic interaction among two aqueous phases results in the formation of coacervates, while ionic interaction conditions at room temperature results in transition from liquid to gel due to ionic gelation.14

Different Application of Nanoparticles

Nanomedicine as nanoparticles and nanospheres has incredible prospects for the improvement of the diagnosis and treatment of human diseases. These are environmentally acceptable procedure for the biosynthesis of nanoparticles is the use of microbes.15

Timed release of the drug

These Nano medicines prevents nonspecific toxicity the drug must not diffuse out of the particle while it is still in the circulatory system, and it must remain encapsulated until the particle binds to the target. On site of disease nanoparticles can be significantly used for targeted drug delivery due to which some foremost influences occurs such as

- Drug bioavailability may improve by using the nanoparticles.
- Targeting of drugs to a specific site can be achieved
- To improve the uptake of poorly soluble drugs
- Chemotherapeutic agents such as dexamethasone, doxorubicin 5-

fluorouracil and paclitaxel have been successfully formulated using nanomaterials.16

Cell specificity

Enrichment of cell specificity by conjugating antibodies to carbon nanotubes with fluorescent also radiolabelling.16

Internalization

It is the internalization within mammalian cells can be achieved by surface functionalized carbon nanotubes.17

Vaccine Delivery

The conjugation with peptides may be used as vaccine delivery structures.17

Gene Silencing

Its highly selective therapy is required in cancer therapy where tumor cells will be selectively amended. Here with small interfering RNAgene silencing has been done. Through targeting functionalized single walled carbon nanotubes by means of siRNA this can be achieved in the targeted cell to silence targeted gene expression.17

In Diagnostics

It has been noticed that compounds that are bound to nanotubes enhance the efficiency of diagnostic methods as well. Such meaning of functionalization and high length to diameter aspect ratio helps in designing the highly efficient biosensors. Because of its physicochemical properties over other drug delivery and diagnostic systems carbon nanotubes offer various advantages. The physicochemical characteristics are high thermal conductivity, ordered structure with high aspect ratio, ultra-light weight, metallic, high electrical conductivity, high mechanical strength or semi metallic behaviour.18

NANOTECHNOLOGY IN MEDICINE

Drug Delivery

As a medicine one application of nanoparticle is presently being developed which involves delivered the drugs, heat, light or other elements to specific types of cells in form of nanoparticles. The nanoparticles are specifically engineered so that they are strained to disease cells, which will permit direct treatment of such cells.19

There are certain nanoparticle drug deliveries applications are described below,

Nanoparticles in Pulmonary Drug Delivery

- The prime function of the lung is to enable the air exchange between blood and external environment, further to maintain homeostatic systemic pH. The big surface area, larger than 100 m2 and the lean barrier between pulmonary lumen and capillaries create suitable conditions for efficient mass transfer.20 Therefore lungs are suitable for both local and systemic drug delivery. For now, nanostructures drug formulations offer many advantages over traditional aerosol powders and liquid pulmonary dose formulations as well. Nanoparticle drug formulations not only can greatly improve the bioavailability of poorly water soluble drugs by its large surface area, but can be mainly formulated to offer improved control over the morphology of dry powder drug formulations.21

Nanoparticle-based Drug Delivery using GI Tract

- The oral delivery is the most desirable routes of drug delivery because of improved patient compliance and ease of administration.22 all these features make oral delivery especially attractive for mass immunization and self-administration of medications. Oral drug delivery formulation often provides a longer shelf-life due to drug stabilization in polymeric matrices. The oral drug delivery systems comprise monolithic matrix tablets, osmotic pumps, biodegradable micro particles and nanoparticles with encapsulated drug, microcapsules, and many more.23

Nanoparticles Drug Delivery to Central Nervous System

- The central nervous system disorders are a major cause of disability and are very difficult to treat due to ineffective drug delivery to the brain.24 the manor treatment obstacle is not drug potency but the physical barriers that render the circulatory routes of delivery ineffective. All these barriers are presented at distinct interfaces including the blood vessels of the brain, the choroid plexus, the arachnoid layer of the meninges, and inside brain tumors.25 Such barriers present bigger problems for peptides, proteins, and oligonucleotides that tend to be larger hydrophilic molecules. But the nanoparticles can potentially conquer these difficulties and are being increasingly applied as drug carriers to deliver drugs to the central nervous system.26

Nanoparticles Drug Delivery to Bone

- Bones are the highly specified form of connective tissue those provides an internal support system and sites of muscle attachment for locomotion activities.27 And also the main source of inorganic ions in the body and actively participates in calcium and phosphorus homeostasis in throughout body.28 Because the structural features and properties of bone provide an exclusive opportunity to target drugs to bone tissue engineering, many novel therapeutic targets have been identified in current years to improve the treatment of bone diseases.29

Applications of Nanoparticles in Immunotherapy

- The vaccines creation is one of the medicine's most important activities.30 Many diseases such as SARS, COVID19, measles, mumps, rubella, diphtheria, tetanus, pertussis, polio and yellow fever are all now under control because of the vaccines. Nowadays supplementary work has focused on using technologies such as recombinant DNA methods to develop DNA and subunit vaccines, as well as conjugates vaccines where a weak antigen is linked to a stronger immunogenic such as a protein or membrane complex.31 Through the development of such new vaccines, there is a critical high demand for novel delivery vehicles as well as new adjuvants as immunity can be limited by vaccine degradation and low loading efficiency. Consequently nanoparticle based drug delivery systems offer several advantages for vaccine delivery.32

Applications of Nanoparticles in Gene Therapy

- In genetic understanding and development, molecular, and cellular sciences, more and more new methods have been achieved to prevention, diagnosis as well as in treatment of diseases.33 A novel approach for treatment as Gene therapy represents designed either to alleviate the genetic defect in cells or to provide additional protective effect.34 For instance, gene therapy strategies for solid tumors can be divided into methods that induce anti-tumor immunity, grant drug sensitivity, restore cellular growth control, or inhibit neo- angiogenesis.35 In in vivo gene delivery, need to develop new delivery carriers which can transport therapeutic genes to a exact region either locally or systemically, in order to efficiently

express encoded proteins at the site targeted.36

Applications of Nanoparticles in Cancer Therapy

A very important impact of nanoparticle-based drug delivery systems emerges to be the localized treatment of solid tumors.37 Advanced nanoparticle delivery technologies offer the opportunity for passive accumulation of intravenously injected nanoparticles ranging between 20-150 nm, from permeable vasculature.38 The nanostructured vehicle can enter into the tumors because of the discontinuous and leaky nature of the tumor microvasculature which contains larger pores ranging between 100-1000 nm in diameter. 39

Diagnostic Techniques

This technique is use full in to make very early detection of cancer tumorseasier, many researchers are developing a nanoparticle intended. Nanoparticles release "biomarkers" molecules when the glue to cancer tumors is detected and the biomarkers are identified as peptides.40This idea is even at initial stages of cancer as each nanoparticle carries several peptides which results in a high concentration of these biomarkers those enabling early detection of the disease.41 The color of the nanorod changes when proteins are accumulating on the nanorods. These tests are designed to be done rapid and inexpensively for early detection of a problem.42

Anti-Microbial Techniques

Many bacterial infections can be fought by a nanoparticle cream which contains nitric oxide gas, known to kill bacteria. Research on mice have promised that using the nanoparticle cream to release nitric oxide gas at the site of staph abscesses significantly reduced the infection.43 If an infection is started by the harmful bacteria releasing the antibiotics, coating with Nano capsules containing antibiotics, burn dressing will open. Faster treatment of an infection can be done which reduces the number of times a dressing has to be changed.44

Respiratory tract

Very common passages for nanoparticles is respiratory tract, Nanoparticles could pass up normal phagocytic defenses within respiratory tract and gain access to systemic circulation and may reach to CNS. The aerosol therapy with nanoparticles as drug carrier is gaining importance for delivering therapeutic compounds.45 Lungs are attractive target for drug delivery due to non- invasive

administration via inhalation aerosols, avoidance of first-pass metabolism, direct delivery to the specific site of action for the treatment of respiratory diseases/disorders and the availability of a huge surface area for local drug action and systemic absorption of drug.46 The colloidal carriers (i.e., Nano carrier systems) in pulmonary drug delivery present many advantages such as the potential to achieve quite uniform distribution of drug dose amongst the alveoli, achievement of improved solubility of the drug from its own aqueous solubility, a sustained drug release which consequently lessen dosing frequency, improves patient compliance, decreases incidence of side effects and the potential of drug internalization by cells.47

Tissue Repair

The tissue repair while using iron oxide nanoparticle is accomplished either through welding, apposing two tissue surfaces then heating the tissues sufficiently for join them, or through soldering, where protein or synthetic polymer-coated nanoparticles are placed between these two tissue surfaces to improve joining of the tissues. The temperatures greater than 50°C are known to induce tissue union that induce by the denaturation of proteins and the subsequent entanglement ofadjacent protein chains.48 This is so believed to be nanoparticles that strongly absorb light corresponding to the output of a laser are also useful to tissue repairing procedures.49 The gold- or silica-coated iron oxide nanoparticles have been designed to strongly absorb light. The nanoparticles are then coated onto the surfaces of two pieces of tissue at the joining site. This is a technique which can be affords methods to minimize tissue damage by using the least harmful wavelengths of light and/or lower powered light sources. 50

CONCLUSION

Because of their incredible properties the nanoparticles have become very significant in many fields in current years such as an energy, healthcare, environment, agriculture etc. Nanoparticle technologies have great potentials, being very much able to convert poorly soluble, poorly absorbed and labile biologically active substance into very much promising and deliverable substances for specially into drug delivery system.

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