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REVIEW ARTICLE

Nano Particles: A Novel System In Current Century

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ABSTRACT

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000 nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. The major goals in designing nanoparticles as a delivery system are to control particle size surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen. For the past few decades, there has been a considerable research interest in the area of drug delivery using particulate delivery systems as carriers for small and large molecules. Particulate systems like nanoparticles have been as physical approach to alter and improve the pharmacokinetic and pharmacodynamic properties of various types of drug molecules. Particle size and surface characteristic of nanoparticle can be easily manipulated to achieve both passive and active drug targeting after parental administration. They have been used in vivo the drug entity in the systemic circulation, restrict access of the drug to the chosen sites and to deliver drug at a controlled and sustained rate to the site of action. Various polymers have been used in the formulation of nanoparticles for drug delivery research to increase therapeutic benefit, while minimizing side effects. Here, we review various aspects of nanoparticle formulation, characterization, effect of their characteristics and their applications in delivery of drug molecules and therapeutic genes.

Key Words: Nanoparticles, liposomes, zeta potential

INTRODUCTION

History

Although nanoparticles are generally considered an invention of modern science, they actually have a very long history. Nanoparticles were used by artisans as far back as the 9th century in Mesopotamia for generating a glittering effect on the surface of pots.

Even these days, pottery from the middle Ages and Renaissance often retains a distinct gold or copper colored metallic glitter. This so called luster is caused by a metallic film that was applied to the transparent surface of a glazing. The luster can still be visible if the film has resisted atmospheric oxidation and other weathering.

The luster originated within the film itself, which contained silver and copper nanoparticles dispersed homogeneously in the glassy matrix of the ceramic glaze. These nanoparticles were created by the artisans by adding copper and silver salts and oxides together with vinegar, ochre and clay, on the surface of previously-glazed pottery. The object was then placed into a kiln and heated to about 600 °C in a reducing atmosphere.

In the heat the glaze would soften, causing the copper and silver ions to migrate into the outer layers of the glaze. There the reducing atmosphere reduced the ions back to metals, which then came together forming the nanoparticles that give the color and optical effects.

Luster technique showed that ancient craftsmen had a rather sophisticated empirical knowledge of materials. The technique originated in the Islamic world. As Muslims were not allowed to use gold in artistic representations, they had to find a way to create a similar effect without using real gold. The solution they found was using luster.

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Michael Faraday provided the first description, in scientific terms, of the optical properties of nanometer-scale metals in his classic 1857 paper. In a subsequent paper, the author (Turner) points out that: "It is well known that when thin leaves of gold or silver are mounted upon glass and heated to a temperature which is well below a red heat (~500 °C), a remarkable change of properties takes place, whereby the continuity of the metallic film is destroyed. The result is that white light is now freely transmitted; reflection is correspondingly diminished, while the electrical resistivity is enormously increased.

For the past few decades, there has been a considerable research interest in the area of drug delivery using particulate delivery systems as carriers for small and large molecules. They have been used in vivo the drug entity in the systemic circulation, restrict access of the drug to the chosen sites and to deliver drug at a controlled and sustained rate to the site of action. Various polymers have been used in the formulation of nanoparticles for drug delivery research to increase therapeutic benefit, while minimizing side effects. Here, we review various aspects of nanoparticle formulation, characterization, effect of their characteristics and their applications in delivery of drug molecules and therapeutic genes.

Definition:

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000nm.The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix.

Depending upon the method of preparation, nanoparticle, nanospheres, nanocapsules can be obtained. Nanocapsules are systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformily dispersed [1,2,3,4].

The major goals in designing nanoparticles as a delivery system are to control particle size surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen. Though liposome have been used as potential carriers with unique advantages including protecting drugs from degradation, targeting to site of action and reduction toxicity or side effects, their applications are limited due to inherent problems such as low encapsulation effiency ,rapid leakages of water soluble drug in the presence of blood components and poor storage stability. On the other hand polymeric nanoparticles offer some specific advantages over liposomes. For instance they help to increase the stability of drugs/proteins and posses useful controlled release properties [5, 6].

The advantages of using nanoparticles as a drug delivery system include the following:

1. Particle size and surface characteristic of nanoparticle can be easily manipulated to achieve both passive and active drug targeting after parental administration.
2. 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.
3. Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents.
4. Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.
5. The system can be used for various route of administration including oral, nasal, parenteral, intra-ocular etc.

Nanoclusters have at least one dimension between 1 and 10 nanometers and a narrow size distribution.

Nanopowders are agglomerates of ultrafine particles, nanoparticles, or nanoclusters.

Nanocrystals are Nanometer-sized single crystals, or single-domain ultrafine particles. Nanoparticle research is currently an area of intense scientific interest due to a wide variety of potential applications in biomedical, optical and electronic fields. The National Nanotechnology Initiative has led to generous public funding for nanoparticle research in the United States.

Preparation Of Nanoparticles:

Nanoparticles can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of matrix materials is dependent on many factors including

- Size of nanoparticles required
- Inherent properties of the drug eg., aqueous solubility and stability
- Surface characteristics such as charge and permeability
- Degree of biodegradability,biocombatibility and toxicity
- Drug release profile desired
- Antigenicity of the final product

Nanoparticles have been prepared most frequency by three methods:

1. Dispersion of preformed polymers
2. Polymerization of monomers
3. Ionic gelatin or coacervation of hydrophilic polymers
4. Supercritical fluid technology
5. Particle replication in non-wetting templates[7,8]

1. Dispersion Of Preformed Polymers:

It is common technique used to prepare biodegradable nanoparticle from poly (lactic acid)(PLA); poly (D,L-glycolide) (PLG); poly(D,L-lactide-co-glycolide) (PLGA) and poly (cyanoacrylate) (PCA)[9,10]. This technique can be used in various ways as described below.

- **Solvent evaporation method:**

In this method, the polymer is dissolved in an organic solvent such as Dichloromethane, Chloroform or Ethyl acetate which is also used as the solvent for dissolving the hydrophobic drug. The mixture of polymer and drug solution is then emulsified in an aqueous solution is then emulsified in an aqueous solution containing a surfactant or emulsifying agent to form an oil in water (o/w) emulsion. After the formation of stable emulsion, the organic solvent is evaporated either by reducing the pressure or by continues stirring. Particle size was found to be influenced by the type and concentration of stabilizer, homogenizer speed and polymer concentration. In order to produce small particle size, often a high speed homogenization or ultrasonication may be employed.

- **Spontaneous emulsification or solvent diffusion method:**

This is a modified version of solvent evaporation method [11]. In this method, the water miscible solvent along with a small amount of the water immiscible organic solvent is used as an oil phase. Due to the spontaneous diffusion of solvents an interfacial turbulence is created between the two phases leading to the formation of small particles. As the concentration of water miscible solvent increases a decrease in size of particles can be achieved.

Both solvent evaporation and solvent diffusion methods can be used for hydrophobic or hydrophilic drugs. In the case of hydrophilic drug, a multiple w/o/w emulsion needs to be formed with the drug dissolved in the internal aqueous phase.

2. Polymerisation Method:

In this method, monomers are polymerized to form nanoparticles in an aqueous solution. Drug is incorporated either by being dissolved in the polymerization medium or by adsorption onto the nanoparticle after polymerization completed. The nanoparticle suspension is then purified to remove various stabilizers and surfactants employed for polymerization by ultracentrifugation and re-suspending the particles in an isotonic surfactant-free medium. This technique has been reported for making polybutylcyanoacrylate or poly (alkylcyanoacrylate) nanoparticles. Nanocapsule formation and their particle size depend on the concentration of the surfactants and stabilizers used [12].

3. Coacervation Or Ionic Gelation Method:

Much research has been focused on the preparation of nanoparticles using biodegradable hydrophilic polymers such as chitosan, gelatin and sodium alginate. Calvo and co-workers developed a method for preparing hydrophilic chitosan nanoparticles by ionic gelation [13,14].The method involves a mixture of two aqueous phases, of which one is polymer chitosan, a di-block co-polymer ethylene oxide or propylene oxide (PEO-PPO) and the other is a polyanion sodium tripolyphosphate.In this method, positively charged amino group chitosan interacts with negative charged tripolyphosphate to form coacervates with a size in the range of nm.Coacervates are formed as a result of electrostatic interaction between to aqueous phases, whereas, ionic gelatin involves the material undergoing transition from liquid to gel due to ionic interaction conditions at room temperature.

4. Supercritical fluid technology:

Conventional methods such as solvent extraction-evaporation, solvent diffusion and organic phase separation methods require the use of organic solvents which are hazardous to the environment as well as physiological systems. Therefore the supercritical fluid technology has been investigated as an alternative to prepare biodegradable micro- and nanoparticles because supercritical fluids are environmentally safe [15].

A supercritical fluid can be generally defined as a solvent at a temperature above its critical temperature,at which the fluid remains a single phase regardless of pressure. Supercritical CO2 is the most widely used supercritical fluid because of its mild critical conditions (TC=31.1 C, PC=73.8 bars), nontoxicity, nonflammability and low price. The most common processing techniques

involving supercritical fluids are supercritical antisolvent(SAS) and rapid expansion of critical solution (RECS).The process of SAS employs a liquid solvent, eg. Methanol , which ti completely miscible with the supercritical fluid to dissolve the solute to be micronized; at the process condition, because the solute is insoluble the supercritical fluid, the extract of liquid solvent by supercritical fluid leads to the instantaneous precipitation of the solute resulting the formation of nanoparticles.

5. Sol-Gel:

The sol-gel process is a wet-chemical technique (also known as chemical solution deposition) widely used recently in the fields of materials science and ceramic engineering. Such methods are used primarily for the fabrication of materials (typically a metal oxide) starting from a chemical solution (*sol*, short for solution) which acts as the precursor for an integrated network (or *gel*) of either discrete particles or network polymers.

Typical precursors are metal alkoxides and metal chlorides, which undergo hydrolysis and polycondensation reactions to form either a network "elastic solid" or a colloidal suspension (or dispersion) – a system composed of discrete (often amorphous) submicrometer particles dispersed to various degrees in a host fluid. Formation of a metal oxide involves connecting the metal centers with oxo (M-O-M) or hydroxo (M-OH-M) bridges, therefore generating metal-oxo or metal-hydroxo polymers in solution. Thus, the sol evolves towards the formation of a gel-like diphasic system containing both a liquid phase and solid phase whose morphologies range from discrete particles to continuous polymer networks.

In the case of the colloid, the volume fraction of particles (or particle density) may be so low that a significant amount of fluid may need to be removed initially for the gel-like properties to be recognized. This can be accomplished in any number of ways. The simplest method is to allow time for sedimentation to occur, and then pour off the remaining liquid. Centrifugation can also be used to accelerate the process of phase separation.

Removal of the remaining liquid (solvent) phase requires a drying process, which is typically accompanied by a significant amount of shrinkage and densification. The rate at which the solvent can be removed is ultimately determined by the distribution of porosity in the gel. The ultimate microstructure of the final component will clearly be strongly influenced by changes implemented during this phase of processing. Afterwards, a thermal treatment, or firing process, is often necessary in order to favor further polycondensation and enhance mechanical properties and structural stability via final sintering, densification and grain growth. One of the distinct advantages of using this methodology as opposed to the more traditional processing techniques is that densification is often achieved at a much lower temperature.

The precursor sol can be either deposited on a substrate to form a film (e.g. by dip-coating or spin-coating), cast into a suitable container with the desired shape (e.g. to obtain a monolithic ceramics, glasses, fibers, membranes, aerogels), or used to synthesize powders (e.g. microspheres, nanospheres). The sol-gel approach is a cheap and low-temperature technique that allows for the fine control of the product's chemical composition. Even small quantities of dopants, such as organic dyes and rare earth metals, can be introduced in the sol and end up in unifromly dispersed in the final product. It can be used in ceramics processing and manufacturing as an investment casting material, or as a means of producing very thin films of metal oxides for various purposes. Sol-gel derived materials have diverse applications in optics, electronics, energy, space, (bio)sensors, medicine (e.g. controlled drug release) and separation (e.g. chromatography) technology.

The interest in sol-gel processing can be traced back in the mid-1880s with the observation that the hydrolysis of tetraethyl orthosilicate (TEOS) under acidic conditions led to the formation of SiO_2 in the form of fibers and monoliths. Sol-gel research grew to be so important that in the 1990s more than 35,000 papers were published worldwide on the process.

Properties Of Nanoparticles:

❖ **Structure:**

Nanoparticles are of great scientific interest as they are effectively a bridge between bulk materials and atomic or molecular structures. A bulk material should have constant physical properties regardless of its size, but at the nano-scale this is often not the case where size-dependent properties are often observed. Thus, the properties of materials change as their size approaches the nano scale and as the percentage of atoms at the surface of a material becomes significant. For bulk materials larger than one micrometer (or micron), the percentage of atoms at the surface is insignificant in relation to the number of atoms in the bulk of the material. The interesting and sometimes unexpected properties

of nanoparticles are therefore largely due to the large surface area of the material, which dominates the contributions made by the small bulk of the material.

An excellent example of this is the absorption of solar radiation in photovoltaic cells, which is much higher in materials composed of nanoparticles than it is in thin films of continuous sheets of material. In this case, the smaller the particles, the greater the solar absorption. Another good example is the bending of bulk copper (wire, ribbon, etc.) occurs with movement of copper atoms/clusters at about the 50 nm scale. Copper nanoparticles smaller than 50 nm, on the other hand, are considered super hard materials that do not exhibit the same malleability and ductility as bulk copper.

Other size-dependent property changes include quantum confinement in semiconductor particles, surface Plasmon resonance in some metal particles and superparamagnetism in magnetic materials. Ironically, the changes in physical properties are not always desirable. Ferroelectric materials smaller than 10 nm can switch their magnetisation direction using room temperature thermal energy, thus making them unsuitable for memory storage.

Suspensions of nanoparticles are possible since the interaction of the particle surface with the solvent is strong enough to overcome density differences, which otherwise usually result in a material either sinking or floating in a liquid. Nanoparticles also often possess unexpected optical properties as they are small enough to confine their electrons and produce quantum effects. For example gold nanoparticles appear deep red to black in solution.

❖ **Surface Area to Volume Ratio:**

Nanoparticles have a very high surface area to volume ratio, which provides a tremendous driving force for diffusion, especially at elevated temperatures. Sintering can take place at lower temperatures, over shorter time scales than for larger particles. This theoretically does not affect the density of the final product, though flow difficulties and the tendency of nanoparticles to agglomerate complicates matters. The large surface area to volume ratio also reduces the incipient melting temperature of nanoparticles.

❖ **Nature of the Production:**

Moreover nanoparticles have been found to impart some extra properties to various day to day products. For example the presence of titanium dioxide nanoparticles imparts what we call the self-cleaning effect, and the size being nanorange, the particles cannot be observed. Zinc oxide particles have been found to have superior UV blocking properties compared to its bulk substitute. This is one of the reasons why it is often used in the preparation of sunscreen lotions.

Clay nanoparticles when incorporated into polymer matrices increase reinforcement, leading to stronger plastics, verifiable by a higher glass transition temperature and other mechanical property tests. These nanoparticles are hard, and impart their properties to the polymer (plastic). Nanoparticles have also been attached to textile fibers in order to create smart and functional clothing.

Metal, dielectric, and semiconductor nanoparticles have been formed, as well as hybrid structures (e.g., core-shell nanoparticles). Nanoparticles made of semiconducting material may also be labeled quantum dots if they are small enough (typically sub 10 nm) that quantization of electronic energy levels occurs. Such nanoscale particles are used in biomedical applications as drug carriers or imaging agents.Semi-solid and soft nanoparticles have been manufactured. A prototype nanoparticle of semi-solid nature is the liposome. Various types of liposome nanoparticles are currently used clinically as delivery systems for anticancer drugs and vaccines.

Effect Of Characteristics Of Nanoparticles On Drug Delivery:

- **Particle Size:**

Particle size and size distribution are the most important characteristics of nanoparticles systems. They determine the in-vivo distribution, biological fate, toxicity and the targeting ability of nanoparticle systems. In addition, they can also influence the drug loading, drug release and stability of nanoparticles

Drug release is affected by particle size. Smaller particles have larger surface area, therefore most of the drug associated would be at or near the particle surface, leading to fast drug release. Whereas larger particles have large cores which allow more drug to be encapsulated and slowly diffuse out [74]. Smaller particles also have greater risk of aggregation of particles during storage and transportation of nanoparticle dispersion. It is always a challenge to formulate nanoparticle with the smallest size possible but maximum stability.

- **Surface Properties of Nanoparticles:**

When nanoparticles are administered intravenously, they are easily recognized by the body immune system and are then cleared by

phagocytes from the circulation34.Apart from the size of nanoparticles, their surface hydrophobicity determines the amount of adsorbed blood components, mainly proteins(opsonins).This in turn influence the in vivo fate of nanoparticles. Binding of these opsonins on to the surface of nanoparticles called opsonization acts as a bridge between nanoparticles and phagocytes. The association of a drug to conventional carriers leads to modification of the drug biodistribution profile,as it is mainly delivered to the mononuclear phagocytes system (MPS)such as liver,spleen,lungs and bone marrow.Indeed,once in the blood stream,surface non modified nanoparticles(conventional nanoparticles)are repeatedly opsonized and massively cleared by the macrophages of MPS rich organs.Generelly, it is lgG,complement c3 components that are used for recognition of foreign substances, especially foreign macromolecules. Hence, to increase the likelihood of the success in drug targeting by nanoparticles,it is necessary to minimize the opsonization and to prolong the circulation of nanoparticles in vivo.

This can be achieved by

(a) Surface coating of nanoparticles with hydrophilic polymers/surfactants;

(b) Formulation of nanoparticles with biodegradable co polymers with hydrophilic segments such as polyethylene glycol(PEG), polyethylene oxide, poly oxomer , poloxamine and polysorbate 80(TWEEN 80).

Zeta potential of a nanoparticle is commonly used to characterize the surface charge property of nanoparticles[16]. It reflects the electrical potential of particles and is influenced by the composition of the particle and the medium in which it is depressed. Nanoparticles with zeta potential above (+/-) 30Mv have been shown to be stable in suspension, as the surface charge prevents aggregation of the particles. The zeta potential can also be used to determine whether a charged active material is encapsulated within the centre of the nanocapsule or adsorbed onto the surface.

- **Drug Loading:**
  A successful nanoparticulate system should have a high drug-loading capacity thereby reduce the quantity of matrix materials for administration. Drug loading can be done by two methods:

❖ Incorporating at the time of nanoparticles production (incorporation method)

❖ Absorbing the drug after formation of nanoparticles by incubating the carrier with a concentrated drug solution (adsorption / absorption technique)

Drug loading and entrapment efficiency very much depend on the solid-state drug stability in matrix material or polymer (solid dissolution or dispersion), which is related to

- The polymer composition
- The molecular weight
- The drug polymer interaction
- The presence of end functional groups(ester or carboxyl)[16-18]

The PEG moiety has no or little effect on drug loading. The macromolecule or protein shows greatest loading efficiency when it is loaded at or near its isoelectric point when it is loaded at or near its isoelectric point when it has minimum solubility and maximum adsorption for small molecules, studies show the use of ionic interaction between the drug and matrix materials can be very effective way to increase the drug loading.

- **Drug Release:**
  To develop a successful nanoparticulate system, both drug release and polymer biodegradation or important consideration factors. In general drug release rates depend on

❖ Solubility of drug

❖ Desorption of the surface bound/adsorbed drug

❖ Drug diffusion through the nanoparticle matrix

❖ Nanoparticle matrix erosion/degradation

❖ Combination of erosion/diffusion process

Thus, solubility, diffusion and biodegradation of the matrix materials govern the release process.

Uses

▪ **Application to the treatment of cancer**

When given intravenously, anticancer drugs are distributed throughout the body as a function of the physicochemical properties of the molecule. A pharmacologically active concentration is reached in the tumor tissue at the expense of massive contamination of the rest of the body. For cytostatic compounds, this poor specificity raises a toxicological problem, which presents a serious obstacle to effective therapy. The use of colloidal drug carriers could represent a more rational approach to specific cancer therapy. In addition, the possibility of overcoming multidrug resistance might be achieved by using cytostatics-loaded nanospheres. The antitumoral efficacy of doxorubicin loaded nanospheres was first tested using the lymphoid leukemia L-1210 as a tumor model. In this study, one intravenous injection of

doxorubicin loaded PIBCA nano spheres was found to be more effective against L1210 leukemia than when the drug was ad ministered in its free form following the same dosing schedule. Although the increased life span (ILS %) of mice injected with doxorubicin-loaded PIBCA nanospheres was twice as high as the IL S % for free doxorubicin, there were no long-term survivors[19].

▪ **Oral Delivery of Peptides and Proteins and Vaccines**

Poly (isobutyl cyanoacrylate) nanocapsules were shown 10 years ago to be able to encapsulate insulin and to increase its activity as assessed by a reduction of glycemia. Several aspects of this phenomenon are surprising: encapsulation of a hydrophilic drug in the oily core of nanocapsules ; reduction of glycemia was only obtained with diabetic animals; hypoglycemia appeared two days after a single administration an d was maintained for up to 20 days depending on the insulin doses, although the amplitude of the pharmacological effect (minimum level of blood glucose) did not depend on the insulin dose [20] .So suggested that nanocapsules could protect insulin from proteolytic degradation in intestinal fluids, based on the protection of encapsulated insulin, observed in the presence of different enzymes invitro. Later studies showed that insulin did not react with the alkylcyanoacrylate monomer during the formation of nanocapsules and was located within the oily core rather than adsorbed on their surface.

Ocular Delivery

The anatomical structure and the protective physiological process of the eye exert a strong defense against ocular drug delivery. This is the reason why conventional ocular dosage forms exhibit extremely low bio-availability. Limited absorption of the drug through the lipophilic corneal barrier is mainly because of short precorneal residence time due to the tear turn-over, rapid naso lacrimal drainage of instilled drug from the tear fluid, and non-productive absorption through the conjonctiva. Only a small proportion (1–3 %) of the applied drug penetrates the cornea and reaches intraocular tissues. For these reasons, it is necessary to develop efficient and more acceptable ocular therapeutic systems.

Subcutaneous /Intramuscular Administration

Subcutaneous administration of nanoparticles was achieved mainly for the delivery of peptides and vaccines. It allows slow release of the entrapped drugs therefore reducing the number of ad ministrations, increasing blood half life of the active drug, and finally, in some cases, reducing side effect.

Nanospheres for oligonucleotide delivery

Oligodeoxynucleotides are potentially powerful new drugs because of their selectivity for particular gene products in both sense and antisense strategies. However, using antisense oligonucleotides in therapeutics is a challenge to pharmaceutical techno logy because of their susceptibility to enzymatic de gradation and their poor penetration across bio logical membranes. Nanoparticulate preparations might be an interesting alternative because of better stability in the presence of biological fluids. In the case of nanospheres made of synthetic polymers [poly(alkylcyanoacrylate), poly(lactic acid)], since oligonucleotides have no affinity for the polymeric matrix, association wi h nanoparticles has been achieve d by ion pairing with a cationic surfactant , cetyltimethylammonium bromide adsorbed onto the nanoparti cle surface[21].

CONCLUSION

Nanoparticles are generally considered an invention of modern science; they actually have a very long history. But in present stage many research are carried out to use the nanoparticles drug delivery system for controlled & targeted release of drugs in the patients to minimize the side effects of the medicaments. In this century we are expecting many products in the market by nanotechnolgy.

REFERENCES

1. Langer R. Biomaterials in drug delivery and issue engineering; one laboratory's experience. Acc chem. Res 2000; 33: 94-101.
2. Bhadra D, Bhadra S, Jain P, NK. Pegnology; a review of PEG – ylated systems. Pharmazie 2002; 57: 5-29.
3. Kommareddy s, Tiwari SB, Amiji MM. Long – circulating polymeric nanovectors for tumor - selective gene delivery. Technology of cancer Treatment 2005; 4: 615 – 25.
4. Lee M, Kim SW. Polyethylene glycol – conjugated copolymers for plasmid DNA delivery. Pharm Res 2005; 22: 1-10.
5. Vila A, Sanchez A, Tobio M, Calvo P, Alonso MJ. Design of biodegradable particles for protein delivery. Journal of Control Release 2002; 78: 15-24.

6. Mu. L. Feng SS. A novel controlled release formulation for the anticancer drug pacitaxel (Taxol (R)): PLGA nanoparticles containing vitamin E TPGS. Journal of Control Release 2003; 86: 33-48.
7. Kreter J. Nanoparticles. In colloidal drug delivery systems, J.K., Ed., Marcel Dekker: New York, 1994; pp 219-312.
8. Reverchon E, Admai R, Nanomaterials and supercritical fluids. The Journal of Supercritical Fluids 2006; 37: 1-22.
9. Rolland JP, Maynor BW, Euliss LE, Exner AE, Dension GM, Desimone JM. Direct fabrication and harvesting of monodisperse, shape - specific nanobiomaterials. Journal American Chemistry. Soc. 2005; 127: 10096 – 10100.
10. Kompella UB, Bandi N, Ayalasomayajula SP. Poly (lactic acid) nanoparticles for sustained release of budesonide. Drug deliv. Technol.2001:1:1-17.
11. Niwa T, Takeuchi H, Hino T, Kunou N, Kawashima Y. Preparation of biodegradable nanoparticles of water - soluble and insoluble drugs with D, L – lactide / glycolide copolymer by a novel spontaneous emulsification solvent diffusion method and the drug release behaviour , Journal of Control Release 1993; 25 : 89 -98.
12. Puglisi g, Fresta M, Giammona G, Ventura CA. Influence of the preparation conditions on poly (ethylcyanocrylate) nanocapsule formation International Journal of Pharmaceutics, 1995; 125; 283 - 287.
13. Alvo P, Renuman-Lopez C, Villa- Jato JL, Alonso MJ. Novel hydrophilic chitosan-polyethylene oxide nanoprticles as protein carriers. Journal of Applied Polymer science 1997-63:125-132.
14. Calvo P, Renuman-Lopez C, Villa- Jato JL, Chitosan and chitosan/ethyleneoxide-propyleneoxide block copolymer nanoparticles as novel carriers for proteins and vaccines. Pharm Res. 1997; 14:1431-1436.
15. Jung J, Perrut M. Particle design using supercritical fluids literature and patent survey. Journal of Supercritical Fluids 2001:20:179-219.
16. Desai MP. Labhasetwar V, Amidon GL, Levy RJ. Gastronitestinal uptake of biodegradable microparticles; effect of particle size, Pharm Res 1996; 13: 1838 – 45.
17. Kroil RA, Pagel MA, Muldoon LL, Roman – Goldstein S, Flamengo SA, Neuwelt EA. Improving drug delivery to intracerebral tumor and surrounding brain in a rodent model; a comparison of osmotic versus bradykinin modification of the blood – brain and / or blood – tumor barriers. Neurosurgery 1998; 43: 879 – 86; discussion 886-9.
18. Kreuter J, Ramage P, V.Hamm S, Gelpernia SE, Engeltardt B, Alyautdin R, von Briesen H, Begley DJ, Direct evidence that polysorbate – 80 - Coated poly (butycyanocrylate) nanoparticles deliver drugs to the CNS via specific mechanisms requiring prior binding of drug to the nanoparticles. Pharm Res 2003 : 20; 409 – 16
19. Brasseur, F.; Verdun, C.; Couvreur, P.; Deckers, C.;Roland, M. Evaluation Expe´rimentale De L'efficacite´ Therapeutique De La Doxorubicine Associe´e Aux Nano-particules De Polyalkylcyanoacrylate, Proceedings of the 4th International Conference on Pharmaceutical Technology, Paris, France , June 3–5, 1986; 177–186.
20. Damge, C.; Michel, C.; Aprahamian, M.; Couvreur, P. New approach for oral administration of insulin with polyalkylcyanoacrylate nanocapsules as drug carrier. Diabetes 1988, 37, 246–251.
21. Fattal , E.; Vauthier, C.; Aynie, I.; Nakada, Y.; Lambert, G.; Malvy, C.; Couvreur, P. Biodegradable polyalkylcyanoacrylate nanoparticles for the delivery of oligonucleotides. J. Controlled. Rel. 1998 , 53, 137–143