Review Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

NANOPARTICULATE DRUG DELIVERY SYSTEM TO IMPROVE SYSTEMIC ABSORPTION-REVIEW

Poonam Kesarwani*[1], Sameer Rastogi[1], Vijay Bhalla[1], Vandana Arora[1]

*[1]School of Pharmacy, Lloyd Institute of Management and Technology, Plot no-11, Knowledge park-2, Greater Noida-201306, India.

ABSTRACT

The nanoparticle is defined as the particulate dispersion (solid particles) within the range of 10 to 1000 nm. Nanocapsules are the capsules in which drug particles are surrounded with thin layer of polymers are called nanocapsules. Drug is encapsulated and dissolution with the polymer matrix by dispersion, matriculation method. Major goals of nanoparticle drug delivery system are to control the release parameter of pharmacological active particle to the specific site of the organs. Circulating particles may be defined as the biodegradable polymeric nanoparticles are coated with the hydrophilic polymer like Polly ethyl glycol (PEG). These are used for potentially absorption of drug store achieve the therapeutic response of the drug. Various polymer are used it may be naturally, synthetic and semi synthetic which provide therapeutic response avoided by its side effect.

KEYWORDS

Nanoparticles, Drug delivery system, Types of nanoparticle, Preparation and Applications.

Author for correspondence:
Poonam Kesarwani,
School of Pharmacy,
Lloyd Institute of Management and Technology,
Plot no-11, Knowledge park-2, Greater Noida-201306, India.

Email: kesarwanipoonam09@gmail.com.

INTRODUCTION

Particulate dispersion of solid particle within size of 10-100 nm are called nanoparticle. Nanoparticulate system can be formed by entrapped and encapsulated with matrix. By these method we can prepared the nanoparticle, nanosphere or nanocapsules. Now a day's biodegradable and inert polymer used as coating agent upon nanoparticle. These coating improve the potential of the drug delivery system[1]. The aim of nanoparticulate drug delivery system is to control the release of drug at

the specific site for longer action. This is achieving by liposome formation which is used as carriers. Carriers have many advantages like protect from the degradation, reduce the toxicity and targeting site of action. Nanoparticles enhance the stability of drug and have the control release property. Most of the drug like Sylimarin and Citosan are fails in clinical trials for good clinical response i.e. they do not reach to the target site of the body. That's why we want to improve the systemic absorption by the nanoparticle drug delivery system by using of nanotechnology method[2]. Sylimarin is a naturally occurring pentacyclic group of triterpenoids found in milk thistle (sylibum maianum).This is used in China, Japan, Germany and other countries for treatment of colon, bladder, lung cancer and liver diseases. Sylimarin is low solubility and high permeability of drug. It has a three isomeric form like, silibinin, silidianin and silicristin. Its main biological active component is silibinin which is highly used for hepatic cancer. Second is that Citosan is a linear aminopolysaccharide.it is composed of Dglucosamine and N-acetyl-Dglucosamine unites. It is obtained by acetylating of citin.it is naturally occurring pollysacharid. The physical and biological properties of Citosan are highly influenced by high molecular weight of acetylation. The derivative of Citosan is (N,N,N trimethyl Citosan), carboxyalkyl citosan, sugar bearing citosan, bile acid modified citosan, thiolated Citosan and cyclodextrin Citosan[3,4]. Nanoparticle drug delivery systems based on penetration of biological barriers and control the release of drug. Nanoparticle should be stable in nanoparticulate drug delivery system. Many polymers are used in this system but polymer should be inert nature and do not interact with drug. Polymers are available in many grads and it is very costly that's why we can use the lipid at the place of polymers and have the several advantages. It reduces the toxicity and interaction with the drug. This lipid, drug particle is known as the lipid nanoparticle[5,6]. Modification and fabrication of polymers is very effective technology which provides the better drug delivery to the system for the treatment of disease. The materials which are used in fabrication are polymers nanostructures. These polymers used with the combination of drug particle and targeted to the site of action. Targeted drug can be conjugated to tissue, ligands or macromolecules to the site of action. Targeted nanoparticulate drug delivery systems are to delivery of anti-cancer, anti-microbial agent, vascular endothelial, brain drug targeting, insulin delivery and neuro disorders[7,8].

TYPES OF NANOPARTICULATE SYSTEM

Polymeric nanoparticles

Polymeric nanoparticles are biodegradable and biocompatible. This is preferred for nanoparticle drug delivery system. They show good potential via chemical modification provide good pharmacokinetic as well as pharmacodynamic control release parameter in drug delivery system. They are providing entrapment and delivery of drug. There are more polymers available like citosan, gelatin, copolymer, polylactic acid, polyglycolicacid, polyalkylcyanoacrylete and polymethylmethacrylate. These polymers are used for preparation of polymer nanoparticle drug delivery system. Polymeric nanoparticle s are colloidal in nature having the size of 10-1000nm.It may be round, branched or shell like structures. Fabrication of nanoparticle is also used for treatment of vaccines and cancer problem. Drugs can be fused with the polymers by different techniques like dissolution, diffusion, attachment, immobilization, dissoption and encapsulation method. These polymeric nanoparticles are used as drug targeting and sustained release at the site of action for better achievement. Namoparticles works as penetration of small particle and enhance the dissolution characteristics. This method is also used for solubility of poorly water soluble drug[9,10]. Polymer nanoparticles is also developed the nanomedicines which is the very useful technique. Biodegradable polymers play the role in body after hydrolysis in to the body and produce metabolic monomers example for lactic acid and glycolic acid. Biodegradable polymer has good compatibility with drug and produce low systemic toxicity[11].

Solid lipid nanoparticle

These are lipid base colloidal carriers like campritol, stearic triglyceride, cetyl palmitate and glycerol tripalmitate with the size of 50-1000 nm. Lipids are well tolerated to the body and having low cost and large production. Lipids are used with the combination of surfactant because it has the stabilize property .These are first come in 1990s as pharmaceutical nanosomes and emulsion. Solid lipid nanoparticles are prepared by the cold homogenization method. These nanoparticles are affected by the campritol 888 ATO and emulsifying agent, 2% lactose and 2% glucose prevent aggregation of nanoparticle by lyophilization process .Lyophilization Method are involved precoated steps, primary drying, secondary drying and final drying. Silibinin loaded nanoparticle in nanometer range which is dispersed in amorphous state and that are used as parental, dermal oral, ocular and pulmonary administration[12,13]. For preparation of lipid nanocapsules, lipid base solvent free formulations are introduced in pharmaceutical industry. This is new process and involved the ethoxylated hydrophilic surfactant which works on temperature and modify in to the inversion phase. In the inversion phase many temperature cycles are applied which reduces the droplet size after that cooling is done and crystallization occurs. This formulation is known as solid lipid stable nanocapsules suspension. This suspension can be stored as freeze dried form. Physicochemical studies of solid lipid nanoparticle can be done by magnetic resonance and electron spin resonance. By the scattering detection we can observe the particle size and flow property. Solid lipid nanoparticles are used for the condensation of the DNA in the lipid which transfers in to the mammalian cells[14,15].

Liposomes

This is drug carriers which are used in nanoparticulate drug delivery system. These are nano, micro and colloidal carriers having the size of 80-100 nm. Liposomes are bilayer. This device which is surrounded by phospholipids and steroid. It is like micelles but micelles monolayer of lipid. Amphiphillic nature of liposome due to modification in surfactant they will form a uniform solution which shows the good biocompatibility. Liposome attaches with cell membrane and transfer the drug by simple endocytosis. Circulatory residence time depends upon polymer. Liposomes are formed by sonication that is lipids are dispersed in to the aqueous media. Liposomes improve the dissolution characteristics and pharmacokinetic parameters[16,17]. Drug is introduced in to the liposome by encapsulation method and achieves the good release of drug from Liposomes; it depends on concentration of lipids or surfactant, pH and osmotic pressure. For the sustained release of drug, increase the concentration of lipids in Liposomes system. There are many Liposomes formulation occurs like anticancer drug, neurotransmitters, antibiotics, anti-inflammatory and anti-arthritis drugs[18].

Nanoemulsions

The nanoemulsions are typically described as thermodynamically stable and translucent/ transparent emulsions that have the droplet size less than 100 nm. The range of nanoemulsions is 50-200 nm. Nanoemulsions present large o/w interfacial areas and radically low interfacial tensions. They have greater capacity to solubilize than solution of micelles. Being thermodynamically stable, nanoemulsions hold an edge over unstable dispersions. The ability of o/w nanoemulsions to integrate hydrophobic drugs into the oil phase lends them more solubility. Nanoemulsions are biocompatible, biodegradable in nature and it is easily prepared by using of carriers. It is more sensitive from hydrolysis with water. Flocculation and sedimentation can occurs if particles are not in nano size. It is metastable in nature. These problems can be avoid by adding of surfactant, surfactant reduce the surface force between two phases and increase the solubilization[19, 20].

Dendrimers

Dendrimers are the macromolecules polymer based nanoparticle. It is formed due to branching of single polymers in to more than two branches. They have symmetric structure and show the functional mechanism. Void space of Dendrimers creates the branching of Dendrimers nanoparticles. The active

site present at the branching site which improves the chemical modification, are utilize their in drug delivery system. The functional group like hydrophilic such as the carboxylic end, it is water soluble end. These hydrophilic groups enhance solubility as well as permeability of drug. Modification in the branching may responsible for the encapsulation of molecules within chemical structure of the Dendrimers[21,22].

Inorganic nanoparticle

Inorganic nanoparticle are based on metals and synthesized but monodipers. This has been used for analysis of images by using of magnetic resonance and high resolution interference. These intrinsic properties have been exposed for many therapies which are very effective and easier to analysis. Metals nanoparticles are able to change the energy in to the heat up to the 70^0C. These heats are utilized for excitation of near infrared and oscillation of magnetic field; both are used in treatment of cancer therapy. [23] Iron oxide nanoparticles are coated with aminosilane in clinical phase 2^{nd} and used for brain cancer and prostate cancer by using of hyperthermia as well as thermoablation methods. Prostate tumor cells are locally killed by magnetic oxide nanoparticle. These small nanoparticle are penetrates the cancerous cells and kill it. Killing process occurs by generation of heats under magnetic field. Silica nanoparticle coated with gold that have absorption ability of heat and works same as iron oxide nanoparticle[24,25]. Nanoparticle technology is better the conventional micron sized particles because nanoparticles have the higher surface area and volume which helps in penetration and solubilization of molecules/atoms. As the particle size decrease, interparicle forces are creates like Vander Waals, electrostatic forces, and magnetic attraction[26].

Preparation of nanoparticle

Nanoparticle can be prepared by four methods which are very useful techniques.

1. Dispersion method
a. Solvent evaporation method
b. Emulsification or solvent diffusion method
2. Coacervation method
3. Polymerization method
4. Supercritical method

Dispersion method

Nanoparticle can be prepared by the dispersion of the biodegradable polymers like PEG, PLA, and PLGA etc. These methods are used in various ways which are given below[27].

Solvent evaporation method

Polymers or matrix are dissolve in organic solvent like chloroform, dichloromethane, ethyl acetate, this makes uniform solution. Organic solvents are also used as dissolving of hydrophobic drugs. This mixture of solution of polymer and drugs is then emulsified in water solution containing surfactant or emulsifying agents to form oil in water emulsion. After the formation of emulsion, organic solvent are evaporated by reducing the pressure or continuous stirring. Size of particles are depends upon concentration of stabilizers, homogenizer speed and nature of polymers[28].

Emulsification or solvent diffusion method

It is new form of solvent evaporation method, it include water miscible solvent along with water immiscible solvent. Spontaneous diffusion of solvent occurs and interfacial turbulence activity is created between the two phases and small-small nanoparticles are formed. If the concentration of water miscible phase is increase then particle size is reduced and obtained the good nature of nanoparticle. Solvent evaporation and solvent diffusion methods are used for both hydrophilic and lipophilic drugs[29].

Coacervation method or ionic gelation method

For the preparation of nanoparticle many biodegradable polymers like chitosan, gelatin and sodium alginates are used in coacervation method. Mixture of chitosan, diblock co-polymer ethylene oxide and polyanion sodium tripolyphoshpate are use in this method. Both phases are aqueous phase. Positively charged of amino group of chitosan interact with negatively charged of tripolyphoshpate and formed coacervates. By the electrostatic interaction ionic gelation of polymer occurs. These ionic interaction occurs between the two aqueous phase at room temperature[30, 31].

Polymerization method

Polymerization occurs between the monomers in aqueous solution and formed polymerized nanoparticles. Drugs can be dissolving during the polymerization or adsorbed after polymerization on the surface of polymers. Before the polymerization, nanoparticle suspension are prepared and then purified to remove the surfactants and stabilizers, after that polymerization will starts by ultracentrifugation and re-suspending the particle in to the ionic surfactant solution[32].

Supercritical method

Nanoparticle can be prepared by the use of supercritical fluid. This is the alternative option for the biodegradable polymers and safe for the environment. Conventional method like solvent evaporation, solvent diffusion and organic phase separation, these create the hazardous to the environment due to the organic solvents[33]. Supercritical fluid is defined as a solvent at temperature above its critical temperature which is remain in a single phase regardless of pressure are called supercritical fluid. CO_2 (SC CO_2) is used as supercritical fluid which is most widely used in pharmaceutical industries and have advantages of low price, nontoxic in nature, and non-inflammable. For the formation of supercritical fluids many processes are involved like supercritical anti-solvent and rapid expansion of critical solution. The process of supercritical anti-solvent methanol is used and it is completely miscible with the supercritical fluid to dissolve the solute at the process condition. Solutes are insoluble in supercritical liquid and extract with supercritical fluid after that precipitation occurs and nanoparticle are formed[34].

Application of nanoparticulate system

Nanoparticle in biology

Nanoparticle detects the biological agent, disease and toxic material. It is very important for the diagnosis of biomedical, forensic and environmental analysis. Biosencer made up of two parts, first is recognition element and transduction element which are responsible for target binding and signaling binding[35]. Oligonucleotide nanoparticle has been detected by the colorimetric biosencers. It is highly sensitive and simple method for detection of nucleotides. Colorimetric biosensor detects the Oligonucleotide sequences which are very useful for the diagnosis of genetic and pathogenic disease. Oligonucleotides can be identify by the general procedure through the fabrication of nanoparticle and fictionalization with single stand DNA. It also detects the amount of products generated by the polymerase chain reaction. This is known as quantifying analysis[36,37]. For the detection of protein, colorimetric biosensor contains led specific "DNAzyme". Other glyconanoparticles have been used for detection of Concanylin A and cholera toxin. Dithiols (C-and N-terminal cysteinyl) peptides are having the properties of bridging agent which is used for colorimetric detection of proteases. Stevens et al. reported that substrate of thermolysin in the combination of cystein amino acid and joined with gold nanoparticle change the system color from blue to red because of presence of thermolysin[38]. Florescence biosensors have been used for the detection of metallic nanoparticle. It is based on Fo^{--} rster resonance energy transfer (FRET) which has the quenching properties. For instance, molecular beacons are sued for the sensing DNA. In this techniques dye molecules is nearest to the nanoparticle surface without target DNA stand because of hairpin DNA structure which leads to fluorescence quenching. Targeted DNA of hairpin structure has open by the hybridization that beneficially composed the catalyst and substrate strand. Substrate strand breaks in to two parts by the Pb, one is head-to-tail and other is tail-to-head[39,40].

Nanoparticle in environmental protection

Nanoparticle has the capability to improve the environmental condition by the nanotechnology like detection, prevention and removing of those materials which are cause the pollution to the environment. These nanotechnologies modified and design the industrial process and achieve the effective products. Many nanoparticles are available for the removal of contamination. For instance, iron nanoparticle and nanosized sensors. Nanotechnology involves the new and unique quality of nanoparticle which is enhancing the catalysts, tunable photo

activity, strength and other characteristics functions[41,42].

Nanotechnology is also involved in water purification for achieving of safe water and this water is used as drinking water. Many disease are developed by the use of polluted water.80% of the bacterial diseases are due to the infected water mainly in India. This is the major goals to removes the all pathogen from drinking water by the nanotechnology[43].

Nanoparticle in medicine

For the treatment of cancer, diabetes, pain, asthama, allergy, infection and many others diseases are cure by the therapeutic and diagnostic agents which are based on the nanoparticulate system. This nanoparticulate system provides modified properties like solubility, diffusion rate, half-life, drug release pattern and absorption characteristics. Nanoparticulate agents give the effective, easier to take low toxicity and increase the products life. Nanoparticles permit the target delivery and controlled release of the drugs; these are concern in the therapeutic delivery system. Nanoparticles also permit the analysis on the molecular level which detects the abnormalities like deutsch of viruses, inflamed cells and disease[44,45].

Nanoparticle as intracellular sustained drug release vectors

Polyhydroxbutyrate (PHB) is used as the intracellular sustained drug release which is come in to the synthetic polymers. These are flexible in nature and provide the facility; efficient drug delivery, make up the biocompatibility and stable formulation[46,47]. Polyhydroxyalkanoates (PHAs) is also used as carrier for the sustained release .PHAs has the 3-Hydroxyalkanoates (3HA) monomers substitutes in the structure which is produce the energy and carbon storage material .PHAs have the physiochemical properties that has been applied in implant biomedical and controlled release applications[48,49]. Poly(R-3-hydroxybutyrate-co-R-3-hydroxyhexanoate) (PHBHHx) have been recently investigate and utilize for biomedical applications but has no longer used for drug control release. PHB and PHBV co-polymer of 3-hydroxybutyrate and 3-hydroxyvalerate are used as extracellular controlled release vectors. PHB and PHBHHx nanoparticle are encapsulating with lipid soluble colorant which are helps to targeting cell for intracellular sustained drug release[50,51].

Nanoparticle as target delivery system

Targeting of nanoparticle drug loaded system to the desired cell or tissue to the body via reducing rate of release .For the targeting drug delivery system; there are two mechanisms can be work i.e. passive and active targeting. For instance; chemotherapeutic agent increases the blood permeability of the cells or tissues. This is the example of passive targeting system and active targeting system permit the surface function of the carriers with ligands which are closely attached with receptors of the cells. The specific targeting nanoparticle work with antibodies and provides selective binding that decrease the toxicity and increase the delivery of the drugs. Targeting nanoparticle has the property of time release of the drug to the circulatory system[52,53]. Nanoparticle targeted drug delivery system also used for receiving of poorly water soluble drug at the site of sction.Anti-cancer drugs like paclitaxel, doxorubicin 5-flurouracil, dexamethasone and many other drugs have been prepared by using of nanoparticle. Polylactic or glycolic acid (PLGA) and polylactic acid (PLA) based nanoparticle have been prepared with the combination of dexamethasone with in intercellular site. Dexamethasone is a chemotherapeutic agent and has the anti-proliferative and anti-inflammatory action on the targeted site. These agents bind with cytoplasmic receptors and form drug-receptors complex is located to the nucleus of the gene which causes the anti-proliferation action.[54]Targeted nanoparticles which are encapsulated produced better bioavailability, low toxicity to the body and cheap in cost. Nanoparticle based drug delivery system is facilitate for hydrophobic and hydrophilic states via oral, vascular and inhalation route of administration[55].

Nanoparticle target ovarian cancer; Small nanoparticle hold the killer gene which are successively suppressing the inflamed tissues of

ovarian mice. These statements are come from the MIT and Lankenau Institute. According to this statements new approaches are come out for the ovarian cancer treatment but it cause the death around more than 1500 death per year in United States due to the diagnosed at last stage of cancer disease. Now a day's new and effective treatments are available which is reported in Aug 1 issue of the journal cancer Research, provides gene that contained the diphtheria toxin, which kill the inflamed cells without harming of proteins. These toxins are arrived from the Corynebacterium diphtheriae[56]. Polymeric nanoparticle helps in release of corticoids and has the property of anti-inflammatory action in the treatment of eye disease like uveitis. Corticoids achieve the good healing process and effective in fibrosis. Topical administration of the corticoids has the fewer side effects than the systemic administration due to the use of small amount of the drug. For the good therapeutic effect, direct inject the drug in to the blood vessels but this administration cannot be repeated because have the hemorrhage problem. Anather techniques is available i.e. implantation; it require desire therapeutic concentration of the drug for release and have the disadvantage because surgical incision is required for install the implant. It cannot be easily removed and have the chance of migrate from their site[57,58].

Nanoparticle in blood brain barrier (BBB)

Blood brain barrier exist between the blood streamline and central nervous system. BBB permits only transfer of ions and conserve the constant osmotic pressure for passage of nutrients. The main function of BBB is to safe the brain and spinal axis from chemical and bacteriological threats. Drug particles cannot be transfer from the tightly endothelial cells of the junction. One technique can be work on drug delivery to the central nervous system is that nanoparticle which are able to pass via endothelial cells due to reduce size of nanoparticle. It gives the good result in treatment of brain tumor[59,60].

Vaccines and gene therapy

Nanoparticle are also helps in delivery of gene and vaccines by encapsulation method, it is secured from the degradation of the pH, bile, enzymes. Gene can be binding on the surface of nanocapsules or nanoparticle for achieving of good durability and stability. Binding should be versatile. Nanoparticle made from the PEG and PMMA which gives the positively charged group and stearic stability. Positively charged group helps to bind with DNA. By using of this method physical desorption problem can be avoid. Gene therapy utilize for medication of neurodegenerative diseases like Parkinson. GNDF (Glial Cell Line-Derived Nerotrophic Factor) is culpable for control delivery of gene in disease. Tyrosine hydroxylase and initial viral vector are also utilized for deliver via gene[61, 62].

Gold nanoparticle in preconcentration and preparation of sample

A new method is come out for the extraction and preconcentration of potable water. The name of this method is solid phase nanoextraction; it shows the good compatibility of polycyclic aromatic hydrocarbons (PAHs) to gold nanoparticle. In this method 500 ml of unpurified water sample is emerged with 950 ml of gold nanoparticle solution, after some time PAHs take absorption on the surface of gold nanoparticle. This is the first step of the method and centrifugation take place in second step and throw out the supernatant after that we collect the adsorbed analytes which is deliver from gold nanoparticle by appending 2ml of 1-pentanethiol and 48 ml of n-octane. The eventuate is explicate either by HPLC or by laser-excited time-resolved Shpol'skii spectroscopy. Preconcentration of aromatic and monohydroxy-PAHs in urine have done via adsorption on surface of gold nanoparticle. This method can be applied for low molecular mass of sample[63]. Gold nanoparticle also assign on concentrated protein from large volume of urine (415 ml) sample. On conflicting, trichloroacetic acid is commonly used and gives no enrichment for protein in urine samples with volume above 2 ml with the concentration of 4 ppm. Moreover, gold nanoparticle - combined protein can be assigned to the gel electrophoresis[64].

Nanoparticle in cosmetics

Nano-emulsions contain two phases and having the size 50-100 nm which is used as cosmetic product in the form of lotion, cream, conditioner etc. Globular vesicles are also used as cosmetic product and having the size of 25-5000 nm. It is constitute by amphiphilic molecules which contained double layer or multi double layers. Liposomes and Noisome are considered in globular vesicles; Liposomes made from phospholipids and nanosomes use non-ionic surfactant like polyoxyethylene alkyl ethers or esters. Vesicles form of the nanoparticle increases the stability and compatibility with skin tolerance compositions like unsaturated fatty acids, vitamins and anti-oxidants. Insoluble; mineral based ingredients are used in sunscreen. TiO_2 is played the important role in sunscreen and having the property of reflection and scatter of UV light with the size of 60-120 nm. Nanoparticles are treated with aluminum oxide or silicon oil for increasing of dispersion property in sunscreen medicament. Silver nanoparticles have the potency to kill the germs which is available in toothpastes, soaps, face creams, food packaging, and clothing. And also used in disinfectants and wound dressings. Nano cosmetics include eye liner, body lotions, bronzer, scrubs deodorants shampoos etc. Gold nanoparticle, silver nanoparticle, padaliumium nanoparticle, and TiO_2 nanoparticles are having the physical and chemical property of skin uptake and carryings activities. Sol-gel, vacuum deposition, ball milling, pyrolysis and other methods are available for the preparation of nano-cosmetics products[65].

Nanoparticle in agriculture

Nanoparticles are used for delivery of pests, nutrients, chemicals, water and hormones to the plants in agriculture. These have been done with the help of nanosensors and nano based delivery systems. Nanosensors work on plant to determine the presence of plant viruses, amount of soil nutrients, fertilization capability, level of plant hormones and environmental pollution. Nano-capsules can be used in crop biotechnology[66].

Supermagnetic nanoparticle in biomedical

Magnetic separations have been done by the Supermagnetic nanoparticle in biomedical and biological research. It is highly delicate technique for the choice of selective tumor cell from blood. For instance; malaria parasite through marking the red blood cells with immunospecific magnetic fluid. The DNA sample has been amplified and identified by polymerase chain reaction using pre-processing technology of Supermagnetic nanoparticle and other techniques is cell counting in which cells are tagged with supermagnet. Those tagging provides the location and number of cells via magnetic moment. Magnetic enzyme linked immunosorbent assay have been done by magnetic nanoparticle. For the determination of number of cells with fluorescent enzyme which is used in magnetic separation method. Target material and magnetic separation are used for increasing of material by the following of initial immobilization[67]. Superparamagnetic iron oxide particles (SPION) have been developed for the treatment of joint diseases in human. Conventional system has the nephrotoxicity, hepatic and gastric problems, in such case the work of seeing prolonged therapy. But also have the problem of incapability to make up the drug concentration in joints due to extra release of synovial fluid. In that case extracorporal magnets are utilize for enhance of residence time of SPION. This therapeutic method can be used for the treatment of chronic and acute joints problem. Rheumatoid arthritis, interaarticular trauma and synovitis are examples of joints diseases[68]. Analysis of atherosclerotic plaques can be done by MRI with the use of SPIONs, which are derived from Powder Technology Laboratory, Swiss Federal Institute of Technology (EPFL), Switzerland (Department of Cardiology and Angiology), University of Freiburg and Germany. Atherosclerotic lesions can be produced from the monocytes which is initiative cells of macrophages. Macrophages are release the releasing mediators (cytokines and chemokines), these mediators are active state of phagocytosis. Atherosclerotic plaque imagines has been produce by the phagocytosis SPIONs of macrophages which have the affinity on inflammation[69].

CONCLUSION

Pharmaceutical and therapeutic properties are modified by nanoparticle drug delivery system. Modifications are creating by embodying of drug particle to the nanocarriers which protect them from the humiliation as well as facilitates the targeting and controlled release. Nanoparticle have been improve the crossing and absorbing power of drug on cellular level of biological system. These systems are used for poorly water soluble drug by nano-particles designing. Physical handling and aggregation are developed from small particles and large surface area of the nanoparticle system. This is the advantages of nanoparticle drug delivery system.

ACKNOWLEDGEMENT

The authors would wish to acknowledge the School of Pharmacy, Lloyd Institute of Management and Technology, Noida, India for providing facilities and encouragements.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Langer R. Biomaterials in drug delivery and tissue engineering: one laboratory's experience, *Acc Chem Res,* 33, 2000, 94-101.
2. Vila A, Sanchez A, Tobio M, Calvo P, Alonso M J. Design of biodegradable particles for protein delivery, *J Control Release,* 78, 2002, 15-24.
3. Bagul R, Mhajan V and Dhake V. New approaches in nanoparticulate drug delivery system, *International journal of current pharmaceutics Research,* 4(3), 2012, 29-38.
4. Wan Chen M, Tan W, PengWang S, Feng Zong Z and Wang T. Advances in the nanoparticle drug delivery system of silymarin, China, *Journal of Chinese Pharmaceutical Sciences,* 5(7) 2012, 1312-1329.
5. Scheffel U, Rhodes B A, Natajaran T K, Wagner H N. Albumin microspheres for study of the reticuloendothelial system, *J Nucl Med,* 13, 1970, 498-503.
6. Jumaa M, Muller B W. Lipid emulsions as a novel system to reduce the hemolytic activity of lytic agents: mechanism of protective effect, *Eur J Pharm Sci.,* 9(3), 2000, 285-290.
7. Kim I S, Kim S H. Development of polymeric nanoparticulate drug delivery systems: evaluation of nanoparticles based on biotinylated poly (ethylene glycol) with sugar moiety, *Int. J. Pharm.,* 257, 2003, 195-203.
8. Damge C, Maincent P, Ubrich, N. Oral delivery of insulin associated to polymeric nanoparticles in diabetic rats, *J. Controlled Release,* 117, 2008, 163-170.
9. Kim I S, Kim S H. Development of polymeric nanoparticulate drug delivery systems: evaluation of nanoparticles based on biotinylated poly (ethylene glycol) with sugar moiety, *Int. J. Pharm.,* 257, 2003, 195-203.
10. Ikuta K, Mori T, Yamamoto T, Niidome T, Shimokawa H, Katayama Y. Development of polymeric drug delivery system for recognizing vascular endothelial dysfunction, *Bioorganic and Medicinal Chemistry,* 16, 2008, 2811-2818.
11. Des Rieux A, Fievez V, Garinot M, Schneider Y J, Preat V. Nanoparticles as potential oral delivery systems of proteins and vaccines: a mechanistic approach, *J Control Release,* 116, 2006, 1-27.
12. Wissing S A, Kayser O, Muller R H. Solid Lipid nanoparticles for parenteral drug delivery, *Advanced Drug Delivery Reviews,* 56(9), 2004, 1257-1272.
13. Jones M C, Leroux J C. Polymeric micelles-a new generation of colloidal drug carriers, *Eur. J.Pharm. Biopharm,* 48(2), 1999, 101-111.
14. Wang J X, Sun X, Zhang Z R. Enhanced brain targeting by synthesis of 3′, 5′-dioctanoyl- 5-fluoro-2′-deoxyuridine and incorporation into solid lipid nanoparticles, *Eur J Pharm Biopharm,* 54, 2002, 285.
15. Sun W, Xie C, Wang H, Hu Y. Specific role of polysorbate 80 coating on the targeting of nanoparticles to the brain, *Biomaterials,* 25(15), 2004, 3065-3071.

16. Sunderland C J, Steiert M, Talmadge J E, Derfus A M, Barry S E. Targeted nanoparticles for detecting and treating cancer, *Drug Dev Res*, 67, 2006, 70-93.
17. Silva R, Ferreira H, Cavaco-Paulo A. Sonoproduction of liposomes and protein particles as templates for delivery purposes, *Biomacromolecules*, 12, 2011, 3353-3368.
18. Paavola A, Kilpelainen I, Yliruusi J, Rosenberg P. Controlled release injectable liposomal gel of ibuprofen for epidural analgesia, *Int J Pharm*, 199, 2000, 85-93.
19. Solans C, Izquierdo P, Nolla J, Azemar N, Garcia- Celma M J. Nano-emulsion, *Current Opinion in Colloid and Interface Science*, 10, 2005, 102-110.
20. Sonneville Aubrun O, Simonnet J T, L'Alloret F. Nanoemulsions: a new vehicle for skin care products, Advances in Colloid and interface Science, 4(12), 2004, 108-109, 145-149.
21. Tang M X, Redemann C T, Szoka F C. Elimination of prions by branched polyamines and implications for therapeutics, *Bioconjugate Chem*, 7, 1996, 703.
22. Lee C C, MacKay J A, Frechet J M, Szoka F C. Chemotherapeutic Evaluation of a Novel Synthetic Tubulysin Analogue-Dendrimer Conjugate in C26 Tumor Bearing Mice, *Nat. Biotechnol*, 23, 2005, 1517.
23. Johannsen M, Gneveckow U, Eckelt L, Feussner A, Waldofner N, Scholz R, Deger S, Wust P, Loening S A, Jordan A. Clinical hyperthermia of prostate cancer using magnetic nanoparticles: presentation of a new interstitial technique, *Int J Hyperthermia*, 21, 2005, 637-647.
24. Johannsen M, Gneveckow U, Thiesen B, Taymoorian K, Cho C H, Waldofner N, Scholz R, Jordan A, Loening S A, Wust P. Thermotherapy of prostate cancer using magnetic nanoparticles: feasibility, imaging, and three-dimensional temperature distribution, *Eur Urol*, 52, 2007, 1653-1661.
25. Hirsch L R, Stafford R J, Bankson J A, Sershen S R, Rivera B, Price R E, Hazle J D, Halas N J, West J L. Nanoshell-mediated near-infrared thermal therapy of tumors under magnetic resonance guidance, *Proc Natl Acad Sci USA*, 100, 2003, 13549-13554.
26. Hiemenz P, Rajagopalan R. Principles of Colloid and Surface Chemistry, *Marcel Dekker Inc.: New York, NY, USA*, 1997, 6-10.
27. Kompella U B, Bandi N, Ayalasomayajula S P. Poly (lactic acid) nanoparticles for sustained release of budesonide, *Drug Deliv. Technol*, 1, 2001, 1-7.
28. Zambaux M, Bonneaux F, Gref R, Maincent P, Dellacherie E, Alonso M, Labrude P, Vigneron C. Influence of experimental parameters on the characteristics of poly(lactic acid) nanoparticle prepared by double emulsion method, *J. Control. Release*, 50, 1998, 31-40.
29. Niwa T, Takeuchi H, Hino T, Kunou N, Kawashima Y. Preparation of biodegradable nanoparticles of water-soluble and insoluble drugs with D, Llactide/ glycolide copolymer by a novel spontaneous emulsification solvent diffusion method, and the drug release behavior, *J. Control. Release*, 25, 1993, 89-98.
30. Calvo P, Remunan-Lopez C, Vila-Jato J L, Alonso M J. Novel hydrophilic chitosan-polyethylene oxide nanoprticles as protein carriers, *J. Appl. Polymer Sci*, 63, 1997, 125-132.
31. Calvo P, Remunan-Lopez C, Vila-Jato J L, Alonso M J. Chitosan and chitosan/ethylene oxide-propylene oxide block copolymer nanoparticles as novel carriers for proteins and vaccines, Pharm Res, 14, 1997, 1431-1436.
32. Boudad H, Legrand P, Lebas G, Cheron M, Duchene D, Ponchel G. Combined hydroxypropyl-[beta]- cyclodextrin and poly(alkylcyanoacrylate) nanoparticles intended for oral administration of saquinavir, *Int J. Pharm*, 218, 2001, 113-124.
33. Jung J, Perrut M. Particle design using supercritical fluids: Literature and patent survey, *J. Supercritical Fluids*, 20, 2001, 179-219.
34. Thote A J, Gupta R B. Formation of nanoparticles of a hydrophilic drug using supercritical carbon dioxide and

microencapsulation for sustained release, *Nanomedicine: Nanotech. Biology Medicine*, 1, 2005, 85-90.
35. Diamond D. Principles of Chemical and Biological Sensors (Ed.: D. Diamond), *John Wiley and Sons, New York, NY*, 1998, 1-18.
36. Elghanian R, Storhoff J J, Mucic R C, Letsinger R L, Mirkin C A. Maximizing DNA Loading on a Range of Gold Nanoparticle Sizes, *Science,* 277, 1997, 1078.
37. Reynolds R A, Mirkin C A, Letsinger R L. Multiple thiol-anchor capped DNA–gold nanoparticle conjugates, *J. Am. Chem. Soc*., 122, 2000, 3795.
38. Guarise C, Pasquato L, De Filippis V, Scrimin P Gold nanoparticles-based protease assay, *Proc. Natl. Acad. Sci. USA*, 2006, 103, 3978.
39. Dubertret B, Calame M, Libchaber A J. Fluorescence-Signaling Nucleic Acid-Based Sensors, *Nat. Biotechnol*, 19, 2001, 365.
40. Sapsford K E, Berti L, Medintz I L, Angew. Materials for fluorescence resonance energy transfer analysis: beyond traditional donor-acceptor combination, *Chem. Int. Ed*., 45, 2006, 4562.
41. Mansoori G A, Vakili-Nezhaad G R and Ashrafi A R. *Int'l J. Pure and Applied Math*. Sci, 2, 2005, 58.
42. Mansoori G A. "Phase Transitions in Small Systems", Proceed. NanoSci. Tech. Workshop, *Kashan Univ.,* May, 2003.
43. US Environmental Protection Agency, 1998b. Microbial and disinfection by-product rules, *Federal Register*, 63, 69389-69476.
44. Brannon-Peppas, L. and Blanchette J O. Nanoparticle and targeted systems for cancer therapy, *Adv. Drug Deliv. Rev*, 56, 2004, 1649-1659.
45. Kawasaki E S and Player A. Nanotechnology, nanomedicine, and the development of new, effective therapies for cancer, Nanomedicine, 1, 2005, 101-109.
46. Langer R and Tirrell D A. Designing materials for biology and medicine, *Nature,* 2004, 428, 487.
47. Eliyahu H, Barenholz Y and Domb A J. Efficacy and safety of dendrimer nanoparticles, *Molecules*, 10, 2005, 34.
48. Steinbuchel A and Valentin H E. Polyhydroxyalkanoate Inclusion Body-Associated Proteins, *FEMS Microbiol. Lett*, 1995, 128, 219.
49. Xiao X Q, Zhao Y and Chen G Q. *Biomaterials*, 28, 2007, 3608.
50. Chen G D and Wu Q. *Biomaterials*, 26, 2005, 6565.
51. Koosha F, Muller R H and Davis S S. T a novel biodegradable microparticulated drug delivery system: on review, *Crit., Rev. Ther. Drug Carrier Syst*, 6, 1989, 117.
52. Costas Kaparissides, Sofia Alexandridou, Katerina Kotti and Sotira Chaitidou. Recent advances in novel drug delivery systems, *International journal of applied research in pharmaceutical sciences*, 2(4), 2010, 29-35.
53. Bilgiçer Z B, Chang H C, Souza-Schorey C D, Smith B and Zhu E Y. Targeted Nanoparticle Drug Delivery, science, 5(2), 2013-2015
54. Sarabjeet Singh Suri, Hicham Fenniri and Baljit Singh. Nanotechnology-based drug delivery systems, *Journal of occupational medicine and toxicology*, 2, 2007, 16.
55. Maureen R. Gwinn and Val Vallyathan. Nanoparticles: Health Effects Pros and Cons Environmental Health Perspectives, 114(12), 2006, 1818-1825.
56. Abhilash M. Potencial applications of nanoparticle, Potential applications of Nanoparticles, *International Journal of Pharma and Bio Sciences*, 6(1), 2010, 9.
57. Young S, Larkin G, Branley M and Lightman S. Severe bacterial endophthalmitis: towards improving clinical, *Clin Exp Ophthalmol*, 29, 2001, 2-6.
58. Tan D, Chee S, Lim L and Lim A. Drug Delivery Implants in the Treatment of Vitreou, *Ophtamology*, 106, 1999, 223-231.
59. Schroeder U, Sommerfeld P, Ulrich S and Sabel B. Non-pharmaceutical public health

interventions fok, *J Pharm Sci*, 87, 1998, 1303-1305.
60. Kreuter J, Alyautdin R, Kharkevich D and Ivanov A. Apolipoprotein-mediated Transport of Nanoparticle-bound, *Brain Res*, 674, 1995, 171 - 174.
61. Cui Z and Mumper R. Nano-microparticles as immune adjuvant, *Pharm Res*, 19, 2002, 939 - 946.
62. Wu K, Meyers C, Bennett J and King M. Azithromycin inhibits nuclear factor-κB activation during lung, *Brain Res*, 1008, 2004, 284 - 287.
63. Wang H Y, Campiglia A D. Potential role of gold nanoparticles for improved, *Anal. Chem*, 80, 2008, 8202 - 8209.
64. Wang A, Wu C J, Chen S H. Enrichment and Detection of Rare Proteins with Aptamer, *J. Proteome Res.*, 5, 2006, 1488 - 1492.
65. Patel A, Prajapati P, Boghara R. Overview on application of nanoparticle in cosmetics, *Asian Journal of Pharmaceutical Sciences and Clinical Research*, 1(2), 2011, 40-55.
66. Yu J X, Li T H. Distinct biological effects of different nanoparticle commonly used in cosmetics and medicine coatings, *Cell Biosci*, 1, 2011, 19.
67. Pankhurst Q A, Connolly J, Jones S K, Dobson J. Applications of magnetic nanoparticle in biomedicine, *J. Phys. D: Appl. Phys*, 36, 2003, R167-R181.
68. Yi-Yan Yang *et al.*, "Frontiers in Research Review: Cutting-Edge Molecular Approaches to Therapeutics Polymeric Core-Shell Nanoparticles for Therapeutics", *Clinical and Experimental Pharmacology and Physiology*, 33, 2006, 557-562.
69. Petri-Fink A *et al.*, "Development of functionalized superparamagnetic iron oxide nanoparticles for interaction with human cancer cells", *Biomaterials*, 26(15), 2005, 2685-2694.

Please cite this article in press as: Poonam Kesarwani *et al.* Nanoparticulate Drug Delivery System To Improve Systemic Absorption-Review, *International Journal of Research in Pharmaceutical and Nano Sciences*, 3(6), 2014, 558- 569.