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RECENT TRENDS IN NANOSCALE DRUG DELIVERY SYSTEMS: A REVIEW

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ABSTRACT

The prominent trends in manufacturing carrier system for chemical, biological and medical application are to make stable non toxic and uniform dimension particles by using various macromolecules. In this aspect the emergency field of nanoparticle enables various approaches towards optimising synthesis protocols and health methodologies. The aim of this study is to overall environment of the intellectual property concerning the development of cancer targeting nanoparticle and various trends. This analysis gives an estimated technology growth that has taken in geographical regions over years. The review presents an updated summary of recent trends in the field of Nano medicine and Nano based drug delivery system through discovery and application of nanomaterial in improving both efficacy and use. The main convert is focused on improving drug delivery efficiencies which are generally described in low disruptions sustainability and accurate and precise targeted delivery control. The aim objectives are bioavailability, satisfactory, accurate consistent dose, lower manufacturing costs and favourable factors. These new approaches can protect drug from external factors like photodegradation, oxidation, etc. These also offers benefits in treating chronic human diseases by site specific and target oriented delivery of precise medicine. Recently there are number of outstanding applications of Nano based medical agents, biological agents in the treatment of various diseases. These can make with the introduction various development with the new trends in the delivery system.

KEYWORDS: Nanomedicine, polymers, bioavailibility, nanobiased, microemulsification.

INTRODUCTION

Nowadays nanoscale structures are widely proposed and attracted many researches for use in cell biology. The significance advances in nanotechnology are the reason for this attraction. Between various issue in the pharmacological field, developing beneficial drug delivery system is one of the most important factors. The main convert is focused on improving drug delivery efficiencies which are generally described in low disruptions sustainability and accurate and precise targeted delivery control.[1]

Nanotechnology offers multiple benefits in treating human diseases by site specific, and targeted delivery of precise medicines. Recently there are number of outstanding applications of the nanomedicines agents in the treatment of various diseases. The current review presents an updated summary of recent advances in the field of nanomedicine and nonbiased drug delivery system through comprehensive of discovery and application of nonmaterial in improving and both efficacy and use. The word nano is derived from "dwarf" (1nm=9-10m). Depending upon the method of preparation nanoparticles, nanospheres or nanocapsules can be obtained. Pharmaceutical nanotechnology has provided more fine tuned diagnosis and focused treatment of disease at a molecular level.[2] NPs are promising vehicles for drug delivery by easy manipulation to prepare carriers with the objective of delivering the drugs to specific target; such an advantage improves the drug safety. Polymer-based nanoparticles effectively carry drugs, proteins, and DNA to target cells and organs. Their nanometer-size promotes effective permeation through cell membranes and stability in the blood stream. Polymers are very convenient materials for the manufacture of countless and varied molecular designs that can be integrated into unique nanoparticle constructs with many potential medical applications.[3]

Advantages of Nano system

Manufacturing Advantages

Nanotechnology is already making new materials available that could revolutionize many areas of manufacturing. For example, nanotubes and nano particles, which are tubes and particles only a few atoms across, and aero gels, materials composed of very light and strong materials with remarkable insulating properties, could pave the way for new techniques and

superior products. In addition, robots that are only a few nanometers in length, called nanobots, and nanofactories could help construct novel materials and objects.

1. Natural polymer: The most commonly used natural polymers in preparation of polymeric nanoparticles are: Sodium alginate, Albumin, Chitosan, Gelatin.

2. Synthetic Polymer: Poly malic acid, Poly (N-vinyl pyrrolidone), Poly (methyl methacrylate), Poly (vinyl alcohol) Poly (acrylic acid) Poly acryl amidePoly (ethylene glycol), Poly (methacrylic acid), Polylactides (PLA).

Chitosan: It Exhibits micro adhesive particles and can be used to act in the light functions. These chitosan based nanomaterials are widely used for continued drug release system for various of systems including nasal, intestinal, eye and pulmonary.[4]

Alginate: This polymer presents final carboxyl group and presents greater micro adhesives strength when compared with cationic and neutral polymers. Patil and Devarafan developed insulin containing alginate nanoparticles with nicotinamide as a permeation agent in order to lower the serum glucose level and raise serum insulin levels in diabetic rats.[5]

Delivery Process and Drug Designing and Drug Mechanisms

With the development of nanomedicine and due to progression of drug discovery, design and drug delivery systems, numerous therapeutic procedures have been proposed and traditional clinical diagnostic methods have been studied. Alsodrug delivery system has gaining importance in modified release of the active ingredients in the body.[6]

Although there are several nanocarriers with different drug release profiles, strategies are currently being formulated to improve the specificity of the nanostructures to target regions of the organism and to reduce the immunogenicity through their coating or chemical functionalization with several substances, such as polymers, natural polysaccharides, antibodies, cell-membrane, and tunable surfactants, peptides, etc. In some cases where drugs do not display binding and affinity with a specific target or do not cross certain barriers (e.g. blood–brain barrier or the blood–cerebrospinal fluid barrier), these ligand-modified nanocarriers have been used to pass through the cell membrane and allow a programmed drug delivery in a particular environment.[7]

Methods for preparation of nanoparticles from dispersion of preformed polymer

Dispersion of drug in preformed polymers is a common technique used to prepare biodegradable nanoparticles from poly (lactic acid) (PLA), poly (D, L-glycolide) (PLG), poly (D, L-lactide-co-glycolide) (PLGA) and poly (cyanoacrylate) (PCA). These can be accomplished by different methods described below.[8]

a) Solvent evaporation
b) Nanoprecipitation
c) Emulsification/solvent diffusion
d) Salting out
e) Dialysis
f) Supercritical fluid technology (SCF)

Recent Developments

Tissue Engineering

It is an interdisciplinary field that applies the principles of engineering and the life sources towards the development of biological substitute that restore maintain or improve tissue function. The use of microspore scaffold the cells are not able to attach properly and at the same time in the micro fibrous scaffold also. But by the use of nanofibrous scaffold each cells can easily attach to thousands of nanofibers as the size of cells in micrometer. By using this, a single cell can attach to thousands of nanofibers that will exactly mimic like extracellular matrix. So the cells on micro fibrous scaffold have a polarized relation with one side of cell attached to the scaffold and other exposed to media. So in comparison cells are more naturally constrained by nanofiboursscaffolds.[9]

Cancer Therapy

Photodynamic cancer therapy is based on the destruction of the cancer cells by laser generated atomic oxygen, which is cytotoxic. A greater quantity of a special dye that is used to generate the atomic oxygen is taken in by the cancer cells when compared with a healthy tissue. Hence, only the cancer cells are destroyed then exposed to a laser radiation. Unfortunately, the remaining dye molecules migrate to the skin and the eyes and make the patient very sensitive to the daylight exposure. This effect can last for up to six weeks. To avoid this side effect, the hydrophobic version of the dye molecule was enclosed inside a porous nanoparticle. The dye stayed trapped inside the Ormosil nanoparticle and did not spread to the other parts of the body. At the same time, its oxygen generating ability has not been affected and the pore size of about 1 nm freely allowed for the oxygen to diffuse out.[10]

METHODS AND DISCUSSION

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By polimerisation monomers it can be prepared by
a) Emulsion
b) Mini emulsion
c) Micro emulsion
d) Interfacial polymerisation
e) Controlled/living radial polymerization

Solvent evaporation: Solvent evaporation was the first method developed to prepare NPs. In this method, polymer solutions are prepared in volatile solvents and emulsions are formulated. The emulsion is converted into a nanoparticle suspension on evaporation of the solvent for the polymer, which is allowed to diffuse through the continuous phase of the emulsion. In the conventional methods, two main strategies are being used for the formation of emulsions, the preparation of single-emulsions, e.g., oil-in-water (o/w) or double-emulsions, e.g., (water-in-oil)-in-water, (w/o)/w. These methods utilize high-speed homogenization or ultrasonication, followed by evaporation of the solvent, either by continuous magnetic stirring at room temperature or under reduced pressure. Afterwards, the solidified nanoparticles can be collected by ultracentrifugation and washed with distilled water to remove additives such as surfactants. Finally, the product is lyophilized.[11,12] Particle size was found to be influenced by the type and concentrations of stabilizer, homogenizer speed and polymer concentration.

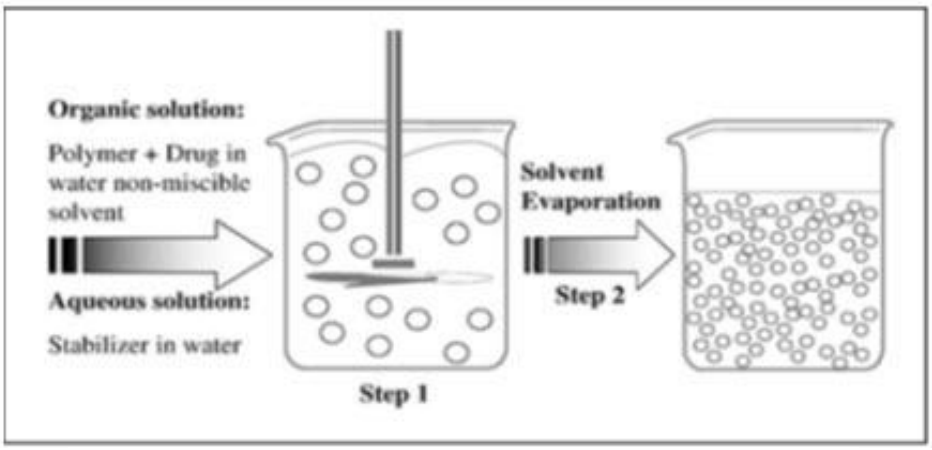

Fig 1: Schematic representation of the solvent-evaporation technique.

Emulsification: This is a modified version of solvent evaporation method.[13] The encapsulating polymer is dissolved in a partially water soluble solvent such as propylene carbonate and saturated with water to ensure the initial thermodynamic equilibrium of both liquids. In fact, to produce the precipitation of the polymer and the consequent formation of nanoparticles, it is necessary to promote the diffusion of the solvent of the dispersed phase by dilution with an excess of water when the organic solvent is partly miscible with water or with another organic solvent in the opposite case. Subsequently, the polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer, leading to solvent diffusion to the external phase and the formation of nanospheres or nanocapsules, according to the oil-to-polymer ratio. Finally, the solvent is eliminated by evaporation or filtration, according to its boiling point. This technique presents several advantages, such as high encapsulation efficiencies (generally >70%), no need for homogenization, high batch-to-batch reproducibility, ease of scale-up, simplicity, and narrow size distribution. Disadvantages are the high volumes of water to be eliminated from the suspension and the leakage of water-soluble drug into the saturated-aqueous external phase during emulsification, reducing encapsulation efficiency. As with some of the other techniques, this one is efficient in encapsulating lipophilic drugs. Several drug-loaded nanoparticles were produced by the ESD technique, including mesotetra(hydroxyl).

Saltingout: In this method the use of potentially toxic solvents is avoided. Here only acetone is used and it can be easily removed in the final step by cross-flow filtration. The preparation method consists of adding, under mechanical stirring, an electrolyte saturated solution containing a hydrocolloid, generally poly (vinyl alcohol) as a stabilizing and viscosity increasing agent to an acetone solution of polymer. After the preparation of an oil-in-water emulsion, sufficient water or an aqueous solution of PEG is added to allow complete diffusion of acetone into the aqueous phase, thus inducing the formation of nanospheres.[14]

Dialysis: Dialysis offers a simple and effective method for the preparation of small, narrow distributed. Polymer is dissolved in an organic solvent and placed inside a dialysis tube with proper molecular weight cut off. Dialysis is performed against a non-solvent miscible with the former miscible. The displacement of the solvent

inside the membrane is followed by the progressive aggregation of polymer due to a loss of solubility and the formation of homogeneous suspensions of nanoparticles.

Super critical fluid technology: The need to develop environmentally safer methods for the production of NP has motivated research on the utility of supercritical fluids as more environmental friendly solvents, with the potential to produce NPs with high purity and without any trace of organic solvent.[15] Supercritical fluid and dense gas technology are expected to offer an interesting and effective technique of particle production, avoiding most of the drawbacks of the traditional methods.

Two principles have been developed for the production of nanoparticles using supercritical fluids.
1. Rapid expansion of supercritical solution.
2. Rapid expansion of supercritical solution into liquid solvent (RESOLV).

Rapid expansion of supercritical solution
In traditional RESS, the solute is dissolved in a supercritical fluid to form a solution, followed by the rapid expansion of the solution across an orifice or a capillary nozzle into ambient air. The high degree of super saturation, accompanied by the rapid pressure reduction in the expansion, results in homogenous nucleation and thereby, the formation of well-dispersed particles. Results from mechanistic studies of different model solutes for the RESS process indicate that both nanometer and micrometer-sized particles are present in the expansion jet.[16] A few studies were carried out on the production of NPs using RESS. Poly (perfluoropolyetherdiamide) droplets produced from the rapid expansion of CO2 solutions. The RESS experimental apparatus consists of three major units: a high-pressure stainless steel mixing cell, a syringe pump, and a pre-expansion unit. A solution of polymer in CO2 is prepared at ambient temperature. The supercritical solution is now allowed to expand through the nozzle, at ambient pressure. The concentration and degree of saturation of the polymer have a considerable effect on the particle size and morphology of the particles for RESS.[17,18]

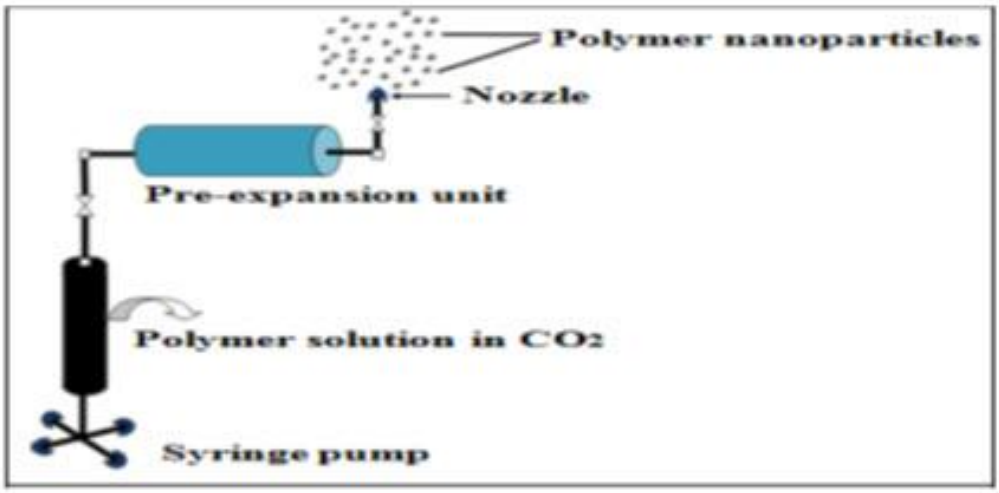

Fig 2: Rapid expansion of supercritical solution.

Rapid expansion of supercritical solution into liquid solvent
A simple, but significant modification to RESS involves expansion of the supercritical solution into a liquid solvent instead of ambient air, termed as RESOLV. Even though in RESS technique no organic solvents used for the formation of NPs, the prime products obtained using this technique are microscaled rather than nanoscaled, which is the main drawback of RESS. In order to overcome this drawback a new supercritical fluid technology known as RESOLV has been developed. In RESOLV the liquid solvent apparently suppresses the particle growth in the expansion jet, thus making it possible to obtain primarily nanosized particles.

Risks in Nanotechnology[19]
Nanoparticles are believed to present the greater risk because: -They are relatively cheap and can be manufactured in large quantities -They are already used in consumer products -Their properties can be very different to the larger forms of the material they are made from -They can be highly reactive.

Uncontrollability: Nanotechnology has changed and will continue to change our vision, expectations, and abilities to control the materials world. These developments in nanoscale will definitely affect the physical and chemical properties of materials. Recent major achievements include the ability to observe structure at its atomic level and measure the strength and hardness of microscopic and nanoscopic phases of composite materials.

Health: It found that most nanotechnologies pose no new risks to humans or the environment. However, much more work need to be done before research can say how

dangerous these nanoparticles could be. For example, it is unclear that nanoparticles would do if they entered the human body. Micrometer-sized clumps of nanoparticles, for example, are relatively unreactive because their surface areas are smaller than that of the same number of individual nanoparticles, and they are too large to enter the blood stream when breathed in. But individual nanoparticles can pass from the lungs into the bloodstream, and are more reactive.

Privacy and Ethical: The most serious risk of nanotechnology comes, not from hypothetical revolutionary materials or systems, but from the uses of evolutionary nanotechnologies that are already developing rapidly. The continuing extension of electronics and telecommunications - fast processors, ultra dense memory, methods for searching databases, ubiquitous sensors, electronic commerce and banking, commercial.

CONCLUSION

Nanotechnologies offer various opportunities and continue to attract a lot of attention because of their potential impacts on a wide range of industries and markets. Consequently, this technology is evolving rapidly and will develop faster over the years. The potential new features of nanotechnology will promote developing the new nano devices. Meanwhile, it is essential to address uncertainties and the potential problems which nanotechnologies may take in an economic and safe manner. The systems like nanoparticles have been used as a physical approach to alter and improve the pharmacokinetic and pharmacodynamic properties with various types of drug molecules. Nanoparticles have been extensively studied as carriers in the industries and medical fields, because they show promise as drug delivery systems as a result of their controlled and sustained release properties.

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