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Synthesis and Physico- Chemical Characterization of Biodegradable Poly-Lactic-Co- Glycolic Acid Nanoparticles

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ABSTRACT

Poly (lactic-co-glycolic acid) (PLGA) is a biocompatible member of the aliphatic polyester family of biodegradable polymers. PLGA has long been a popular choice for drug delivery applications, particularly; it is already FDA-approved for use in humans in the form of resorbable sutures. Hydrophobic and hydrophilic drugs are encapsulated in PLGA particles via single- or double-emulsion. The aim of the study is to evaluate the physico-chemical properties of Polylactidc-co-glycolic acid (PLGA) nanoparticles. Polylactic-co-glycolic acid (PLGA) nanoparticles were synthesized by Double emulsion solvent evaporation method at Department of Animal Biotechnology, Madras Veterinary College. The PLGA nanoparticles were synthesized lyophilized and quantified. The yield of PLGA nanoparticles was 19.2 %. The size of PLGA nanoparticles was measured in the scanning electron microscopy (SEM) and it was found to be 280- 320 nm. The polydispersity index (PDI) of PLGA nanoparticles was 0.192. Net surface charge of the nanoparticles was measured using zetasizer. The measured zeta potential of the PLGA nanoparticles was -2.61 mV.

Key words: *PLGA nanoparticles, Biodegradability, Polydispersity index*

INTRODUCTION

Nanoparticles often present significant adjuvant effects in parenteral vaccine delivery due to their effective uptake by antigen presenting cells. The nanoscaled size allows nanoparticles to be taken up by M-cells in mucosa-associated lymphoid tissue (MALT), i.e., gut-associated, nasal-associated and bronchus-associated lymphoid tissues to initiate vigorous immunological responses[2].

The physical, chemical and biological properties of materials at micro or at nano scale differ fundamentally from those of the corresponding bulk materials. Hence this enables unique interaction with biological systems at the molecular level. Nanoparticles have been prepared from a variety of compounds such as natural or synthetic polymers[9], chitosan[5], gelatin[6], calcium phosphate[4] and so on. The nano or micro particle based vaccine delivery systems offer a number of distinct advantages over conventional vaccines, including prolonged responses, induction of cell mediated and mucosal immunity and a relatively Higher intracellular antigen uptake[7].

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Polymer particles are prepared either from natural or synthetic polymers. Natural polymers (*i.e.* proteins or polysaccharides) have not been widely used for this purpose since they vary in purity and often require cross linking that could denature the embedded antigen. Consequently, synthetic polymers have received significantly more attention in this area. The most widely used polymers for particle-based delivery of vaccines have been Poly Lactic Acid (PLA), Poly Glycolic Acid (PGA), and their copolymer, Poly Lactic-co-Glycolic Acid (PLGA). These polymers are known for both their biocompatibility and resorbability through natural pathways[3].

To meet the need for effective vaccine delivery systems for mass vaccination, Particulate delivery system like PLGA nanoparticles offer promising opportunity to deliver the variety of biomolecules like DNA, protein , peptides. Polylactic-co-glycoloic acid (PLGA) nanoparticles are synthetic polymer prepared from lactic acid and glycolic acid. PLGA is non-toxic, biodegradable, and biocompatible.

Polylacti- co-glycolic acid (PLGA) is the most popular among the various available biodegradable polymers because of its biodegradability, biocompatibility and sustained drug delivery[3]. Polylactic- co-glycolic acid polymers were authorized by Food and Drug Administration (FDA) for drug delivery. Present study focused on synthesis and physico-chemical characterization of PLGA.

MATERIALS AND METHODS

Polylactide co-glycolic acid (PLGA) nanoparticles synthesis

Polylactic-co-glycolic acid (PLGA) nanoparticles were prepared by double emulsion solvent evaporation method as described[9] with some modifications. 100 mg of PLGA dissolved in 4 ml of dimethyl chloromethane (DCM). To this organic phase, 0.5 ml aqueous solution was added slowly while sonication at 25 KHz for 5 min. This primary emulsion was added gradually to 40 ml of 2.5% polyvinyl alcohol (PVA).

This secondary emulsion was kept in a magnetic stirrer overnight at room temperature. PLGA NPs were harvested by high speed centrifugation at 12,000 rpm for 20 min at 4^{o}C. The pellet was washed with triple distilled water. The final pellet was resuspended in sterile PBS (pH 7.2).

Quantification of PLGA nanoparticles

Nanoparticles were lyophilized using 5% trehalose as lyoprotectant. Lyophilized nanoparticles were scrapped aseptically, quantified, labeled and stored at -20^{o}C for further analysis.

$$\text{Yield of PLGA nanoparticles} = \frac{\text{Final yield of PLGA nanoparticles}}{\text{Initial amount of PLGA used for synthesis}} \text{x } 100$$

Morphology of PLGA nanoparticles

The surface morphology of the PLGA nanoparticles was determined by scanning electron microscopy (JEOL, JSM5200, TOKYO, Japan). The lyophilized samples were spread on metal stubs and gold coating was done using an ion-sputtering device. The gold-coated samples were vacuum dried and then examined. Polydispersibility was performed by the instrument.

Zeta potential of PLGA nanoparticles

Zetasizer nano ZS with DTS software (Malvern Instrument Limited, UK). NIBS® (noninvasive backscatter optics) technology was used for the size measurement and net charge of the nanoparticles.

RESULTS

Polylactic-co-glycolic acid nanoparticles synthesis, yield

Polylactic-co-glycolic acid nanoparticles (PLGA) were synthesized by double emulsion solvent evaporation method and the resulting PLGA nanoparticles were lyophilized and quantified. The yield of PLGA nanoparticles was 19.2 %.

Morphology, zeta potential of PLGA nanoparticles

Freeze dried polylactic-co-glycolic acid (PLGA) nanoparticles prepared by double emulsion solvent evaporation method was analyzed by SEM. The observed particles were smooth, spherical in shape with an average size of 286.5 nm under 10.0 KV at 9000 magnification (Fig. 5).

Zeta potential and polydispersity index of PLGA nanoparticles

Blank PLGA nanoparticles were subjected to zetasizer and the size of the PLGA nanoparticles were 312.4 nm and the polydispersity index (PDI) was 0.192. Zeta potential of the blank PLGA nanoparticles was -2.61 mV.

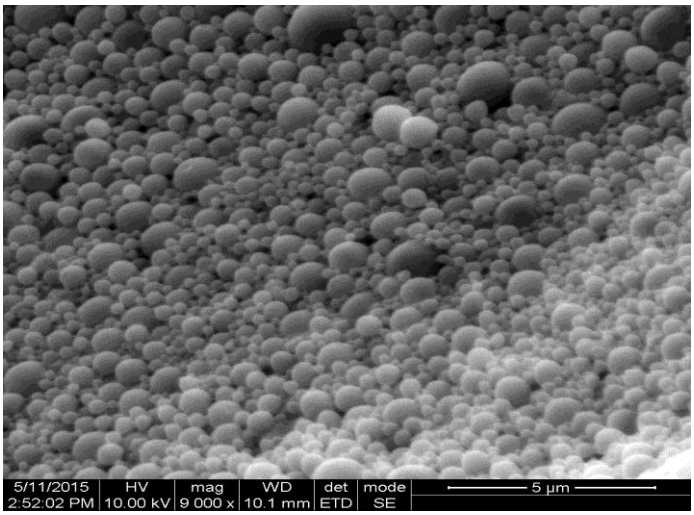

Fig. 1: Morphology of PLGA nanoparticles visualized by scanning electron microscope - Magnification - 9000X

DISCUSSION

Nanoparticle delivery system offers promising opportunity to deliver variety of bioactive compounds such as DNA, proteins, peptides and pharmaceutical drugs to the target site for a long period of time at consistent releasing pattern. Coupling of protein with nanoparticles delivery system improves the efficacy of the immunogenic protein. PLGA isbiodegradable and is widely used for vaccine and drug delivery[1]. Hence, in the present study, a biodegradable PLGA nanoparticle was used as antigen delivery systems to improve the immunogenicity of protein antigen.

PLGA nanoparticles could be synthesized by double emulsion solvent evaporation method. Scanning electron microscopy (SEM) is being used to study the three dimensional structural analysis. SEM image of PLGA nanoparticles showed smooth individual particles with an average size of 286.5 to 320 nm.

Zeta potential represents the net charge of the synthesized PLGA nanoparticles. Zeta potential of the PLGA with fusion protein was +2.61 mV, which indicates that net charge of the PLGA nanoparticles is negatively charged. Negative charge of PLGA nanoparticles is due to presence of lactic acid and glycolic acid moiety present in the PLGA nanoparticles. Zeta potential could combine fusion protein better and slow down the burst release process[8].

CONCLUSION

This study concluded that PLGA nanoparticles synthesized by double emulsion solvent evaporation method has revealed the smooth and spherical appearance of PLGA nanoparticles as viewed in the scanning electron microscopy. This method has also increased the relative homogeneity of PLGA nanoparticles morphology. The yield of PLGA nanoparticles can be further improved by optimizing the parameters like

centrifugation speed use of surfactant and ratio of glycolic acid and lacticacid used for the synthesis of PLGA nanoparticles

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