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Fabrication of Poly Lactic Acid (PLA) Nano/micro Particles and Rods by Electrospraying

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Abstract: *We have fabricated Poly Lactic Acid (PLA) nano/micro particles using the electrospray technique and characterized their morphology and diameter with different process parameters. A continuous liquid jet is electrostatically extruded from a spray source of PLA solution. Due to the surface tension of PLA solution, the extruded jet disintegrates into tiny droplets with diameter ranging from 30nm to a few microns. These droplets were collected at the counter electrode and dried by using hot air at about 50°C for nearly 2 hours. From this investigation, we have found that the morphology and diameter of particles can be controlled by PLA concentration and at the same time the particles can be sorted by varying the deposition distance. Our approach of producing nano/micro PLA particles is not only straight forward but also highly efficient with low production cost. The PLA nano/micro particles are expected to be utilized for the wide range of applications such as controlled drug delivery systems and sensors.*

INTRODUCTION

The enhanced chemical and physical properties of micro and nanoparticles make them ideal for sensors, drug delivery, cosmetics and dyes. The development of biodegradable polymer nanoparticles has become an important research area due to their potential applications in drug delivery systems [1-3]. The material property of PLA has been studied for such applications. The drug release from nanoparticles can be controlled by the polymer composition in the nanoparticles [4]. Studies [2, 5] related to the dimension of nanoparticles suggested their influence on the ease of transportation of these particles and the cellular uptake. [6]. Polymer nanoparticles have been made by using various methods like solvent diffusion [7], solvent displacement [8], salting out [9], interfacial deposition [10], polymerization [11], multiple emulsion [5], nanoprecipitation [1,5], solvent evaporation [2,4] and dialysis [3]. In most of these processes, the size of the nanoparticles is controlled by the addition of a stabilizer, which prevents further aggregation of the particles. Addition of the stabilizer may have an adverse effect on the encapsulated drug. Hence, the choice of the stabilizer gets restricted and its concentration has to be precisely controlled to avoid degradation of the drug. We have previously fabricated nanocups using electrospraying technique without stabilizer [12]. The electrospraying technique [13-15] has been utilized in which a polymer jet is extruded

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from the source by an electrostatic field. This polymer jet splits into tiny droplets due to high surface tension and low viscosity of the polymer solution. The solvent from the droplets evaporates during their transit to the counter electrode, which is a silicon substrate. In this case, unlike the conventional nanoparticle fabrication process, the stabilizer is not required. The smallest diameters of PLA nanoparticles so far has been reported as 100nm [5, 8, 10] previously. In this paper, we report the fabrication of PLA micro/nano particles as small as 30nm and the investigation of the method to control the diameter and morphology with different process parameters.

EXPERIMENTAL SETUP

Chloroform and DCM were the two solvents used to investigate the fabrication process of PLA nanoparticle. Solutions with PLA weight per centage of 0.5, 2, 3 and 5 were prepared in either chloroform or DCM. The particle samples were collected at the counter electrode and then dried in hot air at about 50°C for 2 hours.

The experimental set up is similar to the one described in [11]. It consists of an electrospray source with a syringe needle and a syringe pump, which provided a constant flow rate of 5μl/min of the polymer solution. The distance between the needle and the electrode was set to 7 or 17cm. A negative potential of 4kV in case of chloroform solutions and 5kV in case of DCM solutions was applied between the needle and the counter electrode. This results in the accumulation of surface charges on the surface of the polymer solution droplet at the tip of syringe. The surface charge produced is proportional to the resulting electric field. Along with the outward electrostatic pressure developed by these charges, there exists and inward pressure developed by the surface tension. As the electric field is further increased, the electrostatic forces overcome the surface tension of the solution resulting in the extraction of a liquid jet from the Taylor cone. This extruded polymer jet is separated into small droplets because of surface tension force of polymer solution. These droplets dry in transit and are collected on a silicon substrate.

RESULTS AND DISCUSSION

Figure 1a shows the scanning electron microscope (SEM) image of nanoparticles formed by electrospraying from 0.5% PLA solution by weight in chloroform. The nanoparticles are droplet shaped and nearly 80% of them are less than a micron in size, ref Figure 2a. Further increasing the PLA concentration to 2 per cent resulted in the formation of PLA rods as shown in figure 1b. The length of these rods varied from 10-35 m, while their thickness varied between 3-8 mm. Figure 1c shows the effect of increasing the PLA concentration to 3 per cent. Oval shaped particles are formed but the major axis dimensions are now in micrometers. Nearly 75% of the oval particles had their major axis measured between 6-10 mm. Finally, figure 1d shows the formation of spherical particles with diameters range of microns, after electrospraying polymer solution with 5% PLA concentration. More than 50% of the particles had diameter around 14 m, ref. figure 2b. The formation of rods at low concentrations of PLA may be explained in the following way. At low concentration levels, the effect of increase in the PLA concentration is more pronounced on the viscosity than the surface tension. But since this viscosity is

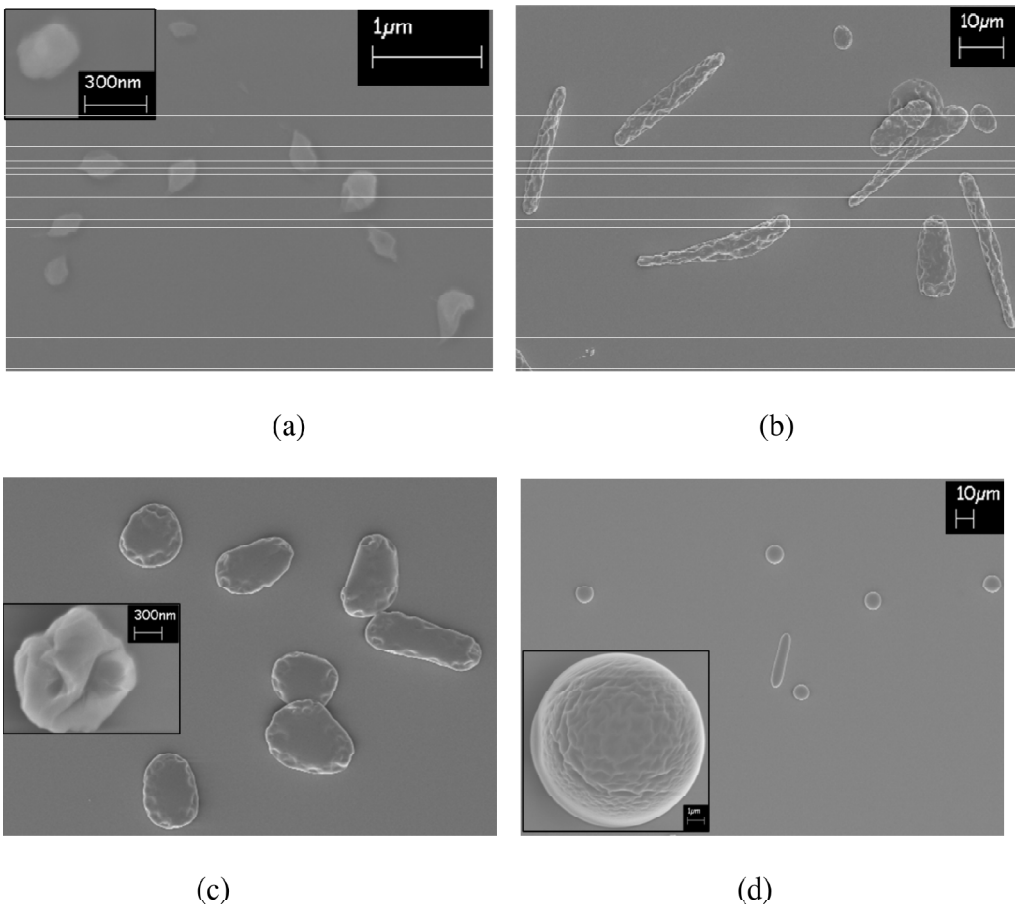
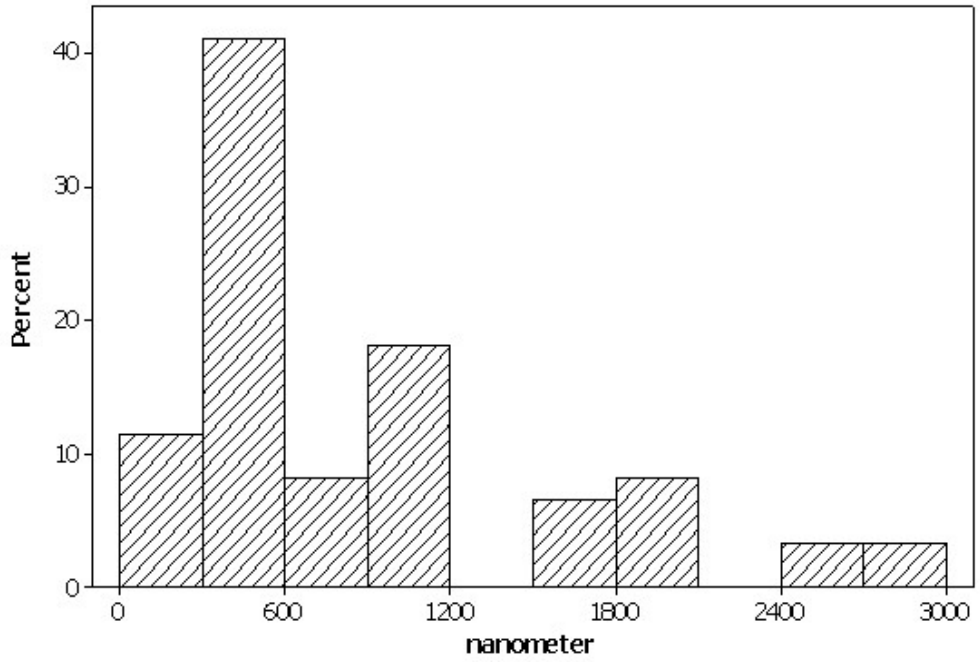


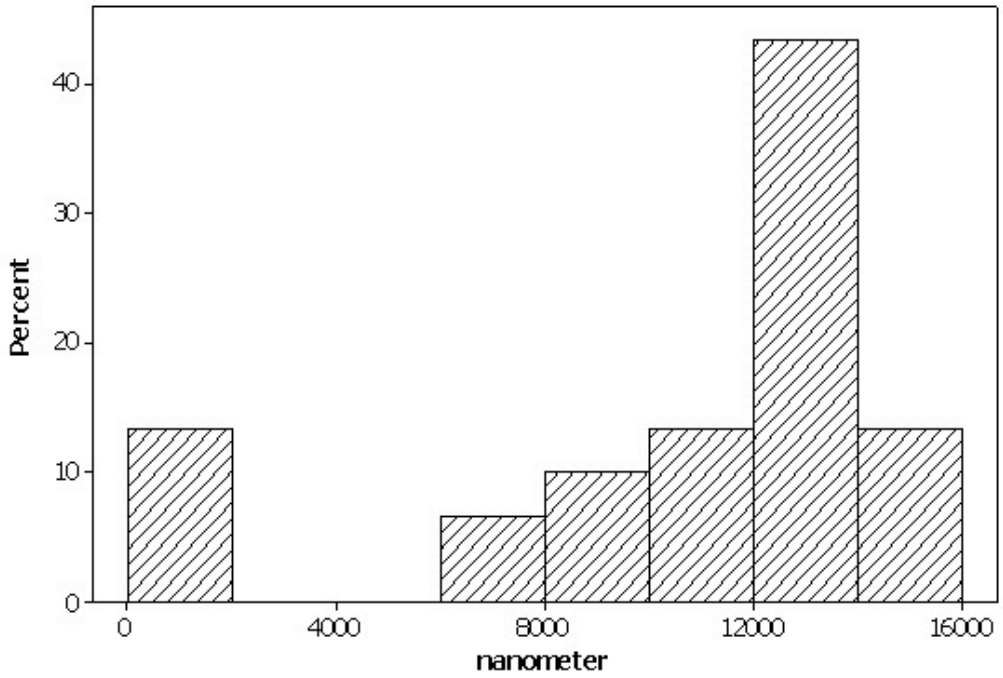
Figure 1: PLA particles using chloroform with (a) 0.5% PLA (b) 2% PLA (c) 3% PLA (d) 8% PLA

not sufficient to form fibers, it results in rod shaped structures. As the concentration is further increased, the surface tension takes over and results in the formation of spherical microparticles. These particles were calcinated by exposing to hot air at about 50°C for a couple of hours. The surface of a dried particle is very rough as seen in figure 1c. This is due to the evaporating the solvent from the surface particles.

Figure 2c shows the mean diameter and the standard deviation of PLA particles formed using chloroform as the solvent The mean diameter for 0.5%, 2%, 3% and 8% PLA concentration is 0.7mm, 3.1mm, 8mm and 10.2mm respectively. The next sets of experiments were investigated with DCM as the solvent. The particle diameter distribution is almost the same as in the earlier case. But, there is the difference in the morphology of the particles. Figure 3b shows the rods formed by electrospraying 2% PLA concentration solution. The rod formation in the case of DCM is seen even for 5% concentration though the mean axial length decreases as the concentration is increased. The mean


Percent
40
30
20
10
0
0
600
1200
1800
2400
3000
nanometer

(a)


Percent
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10
0
0
4000
8000
12000
16000
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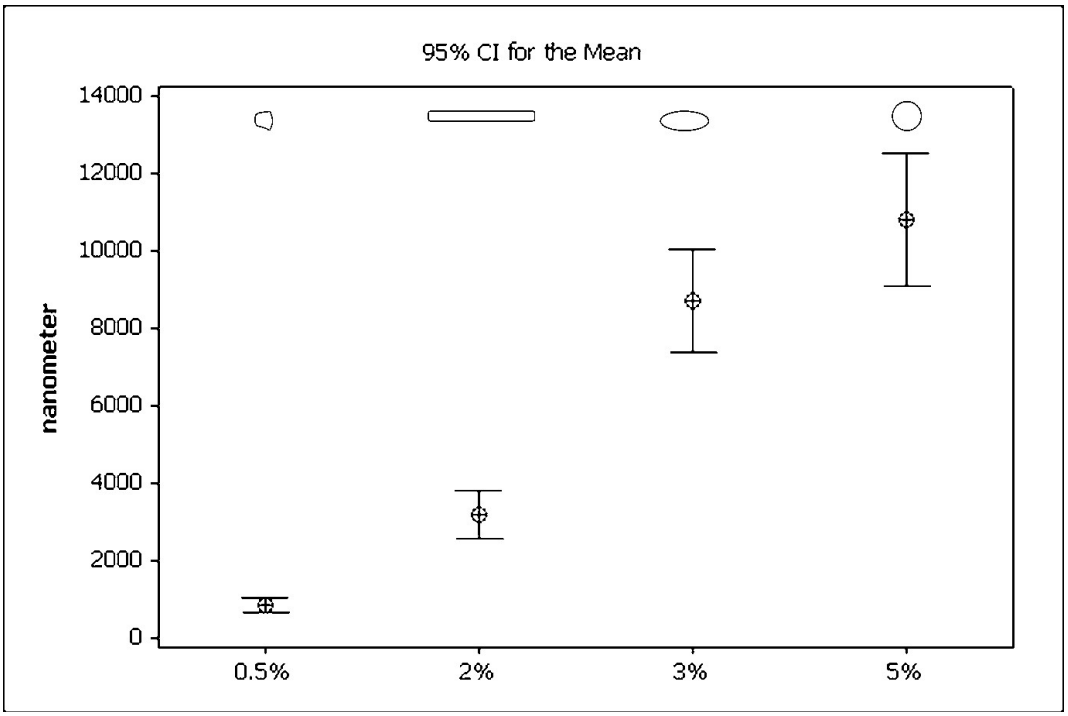
(b)



(b)

Figure 2: Chloroform as solvent and collector distance of 7cm with (a) 0.5% PLA (b) 8% PLA (c) standard deviation plot

particle diameter for the four different PLA concentrations was 700nm, 900nm, 650nm and 1050nm, ref. figure 4. As compared to the earlier case of using chloroform, a significant reduction in the mean diameter is observed by using DCM.

The effect of the deposition distance on the morphology of the particles was also studied. Too small deposition distance resulted in making flattened particles. This can be explained by the fact that the solvent does not have enough time to evaporate during the transition from the source to the substrate. Hence, the particles remaining in a semi fluid state at the time of impact with the substrate results in its flattened shape. Increasing the deposition distance to 17cm resulted in particles with diameter within the range of 30nm to 150nm, ref. figure 5. Further investigation showed that more than 85% of the particles were under 100nm with the highest per centage of 96% occurring with 2% PLA. The result of increasing the deposition distance reduced the standard deviation of the particle distribution which is very important for applications like drug delivery which is highly depend upon the particle diameter.

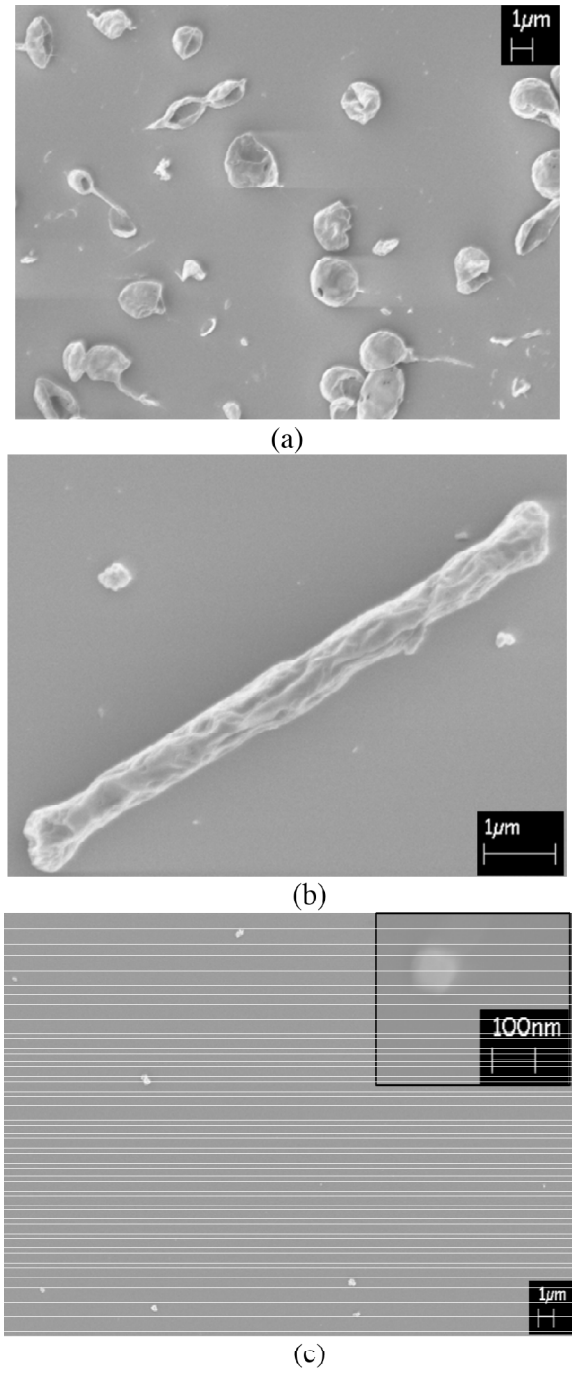


Figure 3: DCM as solvent with (a) 0.5% PLA and collector distance of 7cm (b) 2% PLA and collector distance of 7cm (c) collector distance of 17cm. Notice that the larger particles are all filtered

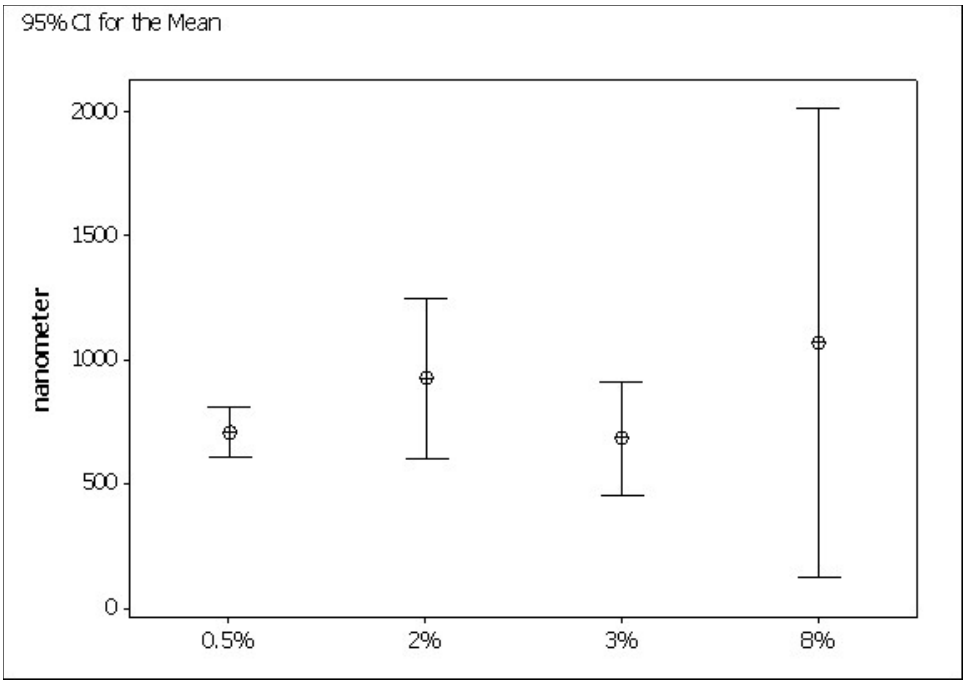


Figure 4: standard deviation plot with DCM as solvent and collector distance of 7cm

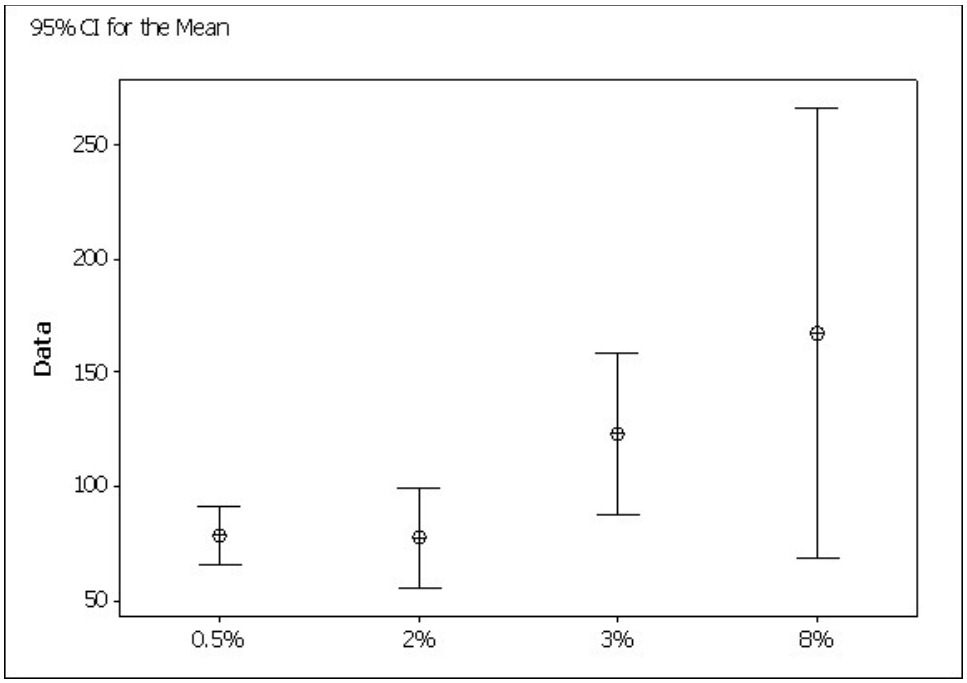


Figure 5: standard deviation plot with DCM as solvent and collector distance of 17cm

CONCLUSION

In this report, we found that the diameter of the PLA nanoparticles can be easily controlled by varying the PLA concentration. Sorting nanoparticles with small diameters is also performed by changing the disposition distance. These PLA particles find wide application such as controlled drug delivery by functionalizing the surface. Small diameter particles are required for short time drug release, where as for a sustained drug delivery over a long time, the size of the particles should be larger. The morphology of the particles can be controlled by PLA concentration. As the concentration was increased, the morphology changed from droplet shaped particles to rods and finally to spherical particles. This is a simple and efficient technique of fabricating nanoparticles which can prove to be very useful to embed drugs for applications like drug delivery.

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