powerful tools for precise engineering of Viatel™ diblock nanoparticle size: polymer and solvent structure

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purpose

nanomedicine has immense potential as it offers nanoparticle(NP)-based delivery vehicles for vaccines or APIs. Polymeric NPs have been used for drug delivery due to their biocompatibility, biodegradability and potential to provide customized properties by tailoring polymer chemistry. NP size is a critical factor that impacts circulation time, in vivo biodistribution and cell uptake[1-3]. Also, NPs < 200 nm can be sterile filtered. Thus, it is crucial to control NP size. Herein, we determined the most effective factors to control NP size[4].

method

polymeric NPs were made by nanoprecipitation (illustrated in figure 1). Two compositions of an amphiphilic bioresorbable diblock copolymer marketed by Ashland Inc., Viatel™ DL 03 PEG5K, methoxy poly(ethylene glycol)-b-poly(D,L-lactide) were used. Each had a PEG length of 5 kDa but varying PLA:PEG ratio (60:40, 75:25 wt%).

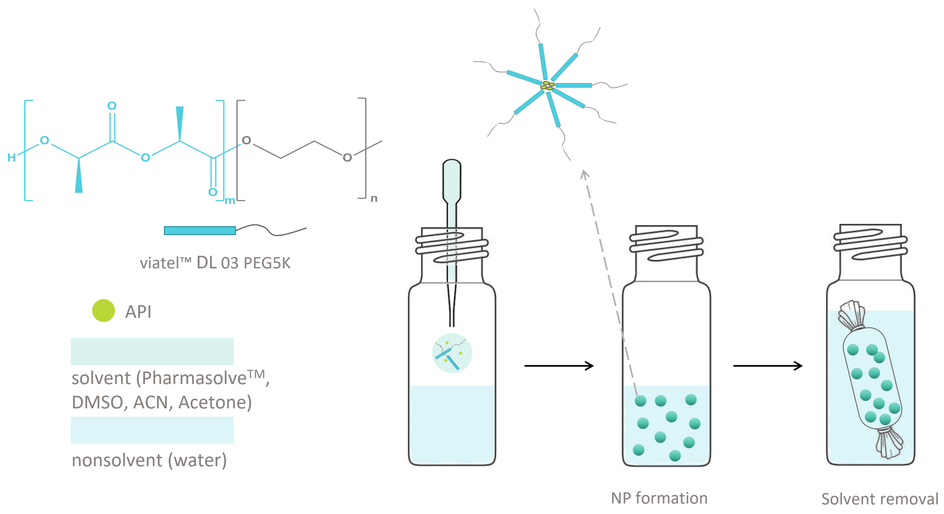

figure 1. nanoparticle formation method, nanoprecipitation

table 1 provides nanoprecipitation conditions in detail. dynamic light scattering (DLS) method was used to measure NP size. NPs were imaged by transmission electron microscope (TEM). API loaded NPs were lyophilized, dissolved in ACN and assayed with HPLC to determine API loading.

table 1. nanoprecipitation parameters	
polymer concentration in organic solvent	20 mg/mL
API concentration in organic solvent	2 mg/mL
solvent/nonsolvent volume ratio	0.1
main solvent	acetone

results

figure 2 shows the size distribution results for both polymers using 100% acetone as solvent. TEM images in figure 3 showed spherical monodisperse morphology for these NPs.

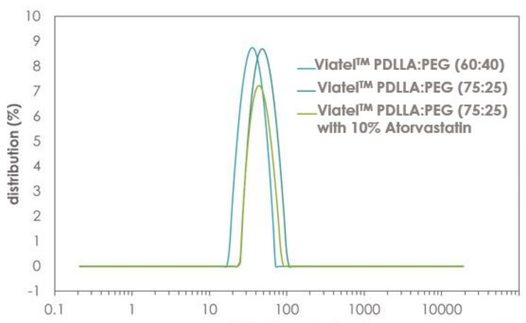

figure 2. size distribution of polymeric NPs.

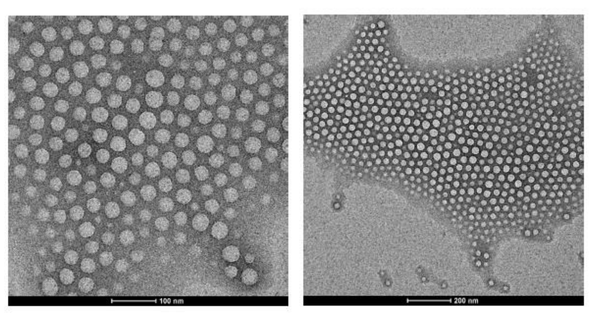

figure 3. TEM images of lyophilized Viatel™ NP using 5% Cavitron™ W7HP5 as lyoprotectatnt

ACN exhibits similar behavior as acetone (Fig 4.A). Increasing NMP content led to formation of larger NPs when using PLA-PEG(75:25) (Fig 2.B). The strongest effect was observed for DMSO(Fig 4.C). It increases NP size to 192.95 nm with PLA-PEG(75:25). Fig 4. D compares the effect of all solvents on NP size.

table 2 summarizes characterization data for API loaded Viatel™ PDLLA:PEG (75:25). Target API loading for these NPs was 10%. Figure 5 shows *in vitro* release profile of the model API (Atorvastatin from NPs over 48 hours.

table 2. API loaded NP characterization	
size (d.nm)	45.49±0.46
PDI	0.089
ζ (mV)	-0.9±0.3
EE(%)	91%

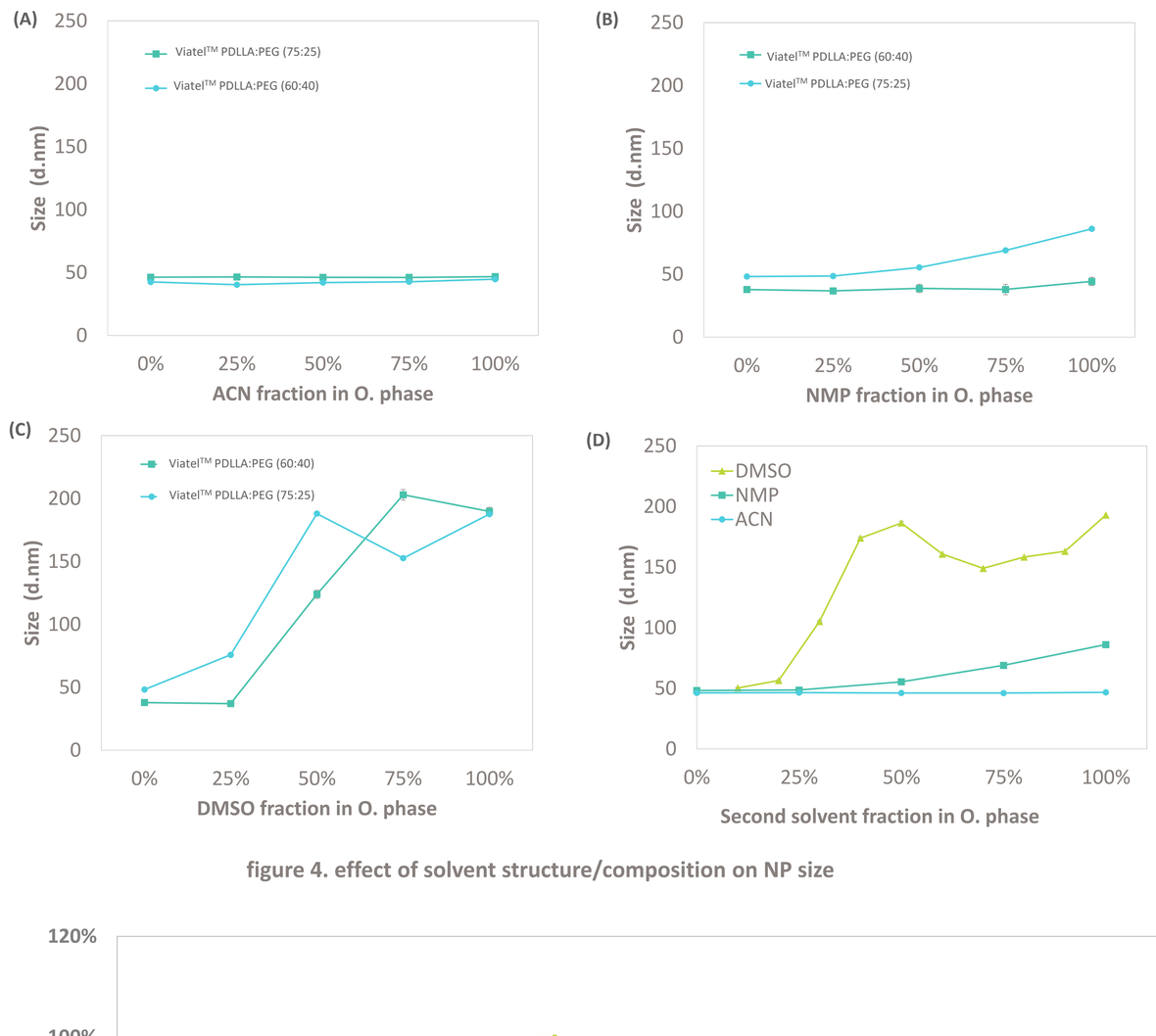

figure 4. effect of solvent structure/composition on NP size

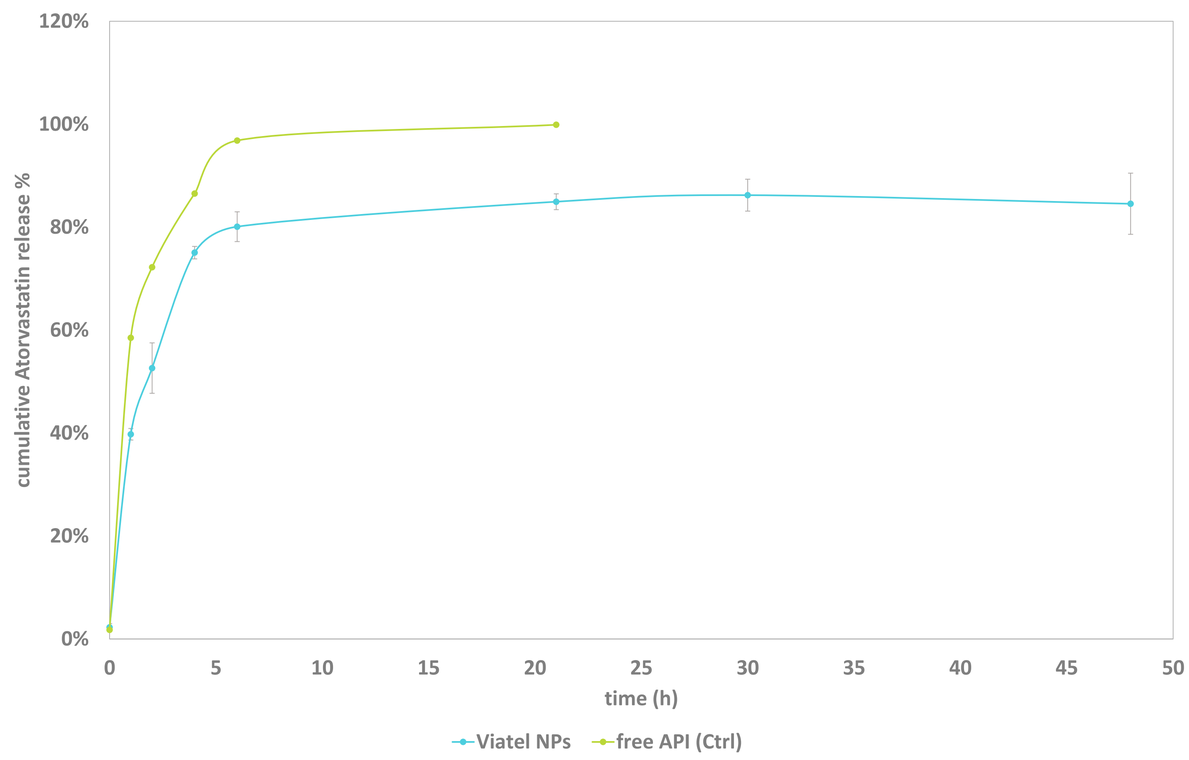

figure 5. *in vitro* release profile of model API (Atorvastatin) from Viatel™ NPs

conclusion

PLA-PEG NP size can be adjusted with two main parameters: polymer structure and solvent choice. Increasing the hydrophobic fraction of the polymer results in formation of larger NPs. Introducing DMSO and NMP into the polymer solution has a significant effect on NP size. As the content of the second solvent increases NP size increases too. Combination of these two parameters allows to precisely design and produce NP with a wide range of diameters.

references

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