Thermal stability of a cationic solid lipid nanoparticle (cSLN) formulation as a possible biocompatibility indicator

Anna Fàbregas, Montserrat Miñarro, Josep Ramon Ticó, Encarna García-Montoya, Pilar Pérez-Lozano, Josep Mª Suñé-Negre

Drug Development Service (SDM). Dept. Pharmacy and Pharmaceutical Technology. Faculty of Pharmacy (Universitat de Barcelona), Avda. Joan XXIII, s/n 08028, Barcelona, Spain
afabregas@ub.edu

Abstract

Cationic solid lipid nanoparticles have become a non-viral delivery system for nucleic acid transfection and further genomic regulation and delivery of encapsulated drugs [1].
A formulation of cationic solid lipid nanoparticles intended for gene delivery [2] has been analyzed in terms of thermal stability at different temperatures. The aim is to determine in a short-term study the influence of temperature on particle size and surface potential, in order to assess what is the best temperature that contributes to maintain cSLN without or low aggregation and proper surface potential [3]. Short-term thermal storage study can serve as well for an approach to behavior at physiological temperature when the study is carried out at 37 ºC.

The cSLN formulation consists of stearic acid, octadecylamine and surfactant Poloxamer 188 [2].
Thermal behaviour is studied at 4 ºC, 25 ºC and 37 ºC.
The cSLN are synthesized using the hot microemulsification method [4]. Then, the nanoparticles are distributed in vials and stored at the temperatures mentioned above. The particle size determinations are carried out in a Mastersizer 2000 laser diffractometre (Malvern Instruments, UK) and Z potential values are determined on a Zetasizer Nano-Z (Malvern Instruments, UK). Both measures are performed daily during a week.

The results are represented graphically (figure 1), and show the evolution of this formulation at the different temperatures in terms of particle size (given as surface weighted mean in nm) and surface charge (given as Z potential in mV). Mean value and standard deviation (table 1) show that at 37 ºC, these nanoparticles suffer the lowest variation both in particle size and Z potential.
Thus, cSLN formulation presents a thermal behavior which results in a stable state at 37 °C in comparison to 25 ºC and 4 ºC, with particle size and Z potential showing slightly changes, then indicating that at this temperature the formulation is still able during a week for acid nucleic binding. Additionally, while 37 ºC corresponds to physiological temperature at which cSLN would be administered, it may be taken into consideration as a possible indicator of biocompatibility, although the influence of other variables such as thermal behavior after nucleic acid binding should be taken into account in further studies.

It can be concluded that regarding low tendency to aggregation or modification of surface potential in the first days after its synthesis when stored at 37 ºC, these cSLN may represent a proper non-viral delivery system following nucleic acid binding intended for immediate and short-term administration.

References

[1] Ekambaran P et al., Scientific & Chemical Communications, 2 2012 80-102.
[2] Fàbregas et al., International Journal of Pharmaceutics, 1-2 2014 270-279.
[3] Vauthier C et al., European Journal of Pharmaceutics and Biopharmaceutics, 2 2008 466-475.
[4] Mehnert W et al. Advanced Drug Delivery Reviews, 64 2012 83-101.

Figure 1. Graphical representation of changes on particle size and surface potential as a function of time.

	Surface weighted mean (nm)				Z Potential (mV)			
Days	4 ºC	25 ºC	37 ºC		Days	4 ºC	25 ºC	37 ºC
1	269	217	236		1	27.7	35.8	32.5
2	124	339	119		2	29.9	35.6	30.1
3	126	55194	113		3	27.1	24.0	31.6
4	237	40709	132		4	34.9	39.2	34.2
5	206	126742	121		5	38.6	37.0	35.2
6	65070	58070	122		6	34.2	43.7	40.2
7	86870	75887	282		7	29.9	31.6	27.3
Mean	**21843**	**51023**	**161**		Mean	**31.7**	**35.3**	**33.0**
SD	**37507**	**44112**	**68**		SD	**4.2**	**6.2**	**4.1**

Table 1. Values of particle size and surface potential at different temperatures during 7 days.