Physicochemical characterization of solid lipid nanoparticles for dimethylfumarate release

GISELA BEVILACQUA ROLFSEN FERREIRA DA SILVA (1,2); ANSELMO GOMES DE OLIVEIRA(1); FABIO DE LIMA LEITE (2)

(1) Universidade Estadual Paulista – Campus de Araraquara - Faculdade de Ciências Farmacêuticas.
(2) Universidade Federal de São Carlos – Campus de Sorocaba.

BACKGROUND

Multiple sclerosis (MS) is a chronic autoimmune inflammatory disease that produces neuroinflammation and demyelination in the central nervous system (CNS). Oral administration of dimethylfumarate (DMF) is able to reduce both the relapse of patients with MS and the formation of new lesions in the white matter. However, the DMF clinical utility can be hindered by poor retention of the drug in the CNS and also the complexity of its transport to the blood-brain barrier (BBB). Solid lipid nanoparticles (SLN) can selectively reaching the brain and carry water-insoluble drugs, such as DMF. The intranasal route (IN) is considered an alternative which more efficiently allows the effect of drugs on the CNS, since the drug to cross the BBB and is not subjected to first pass hepatic metabolism. Due to the activity of DMF in MS and in view of its low solubility in water, there is a need to develop a nanostructured carrier capable of overcoming the BBB and direct it to the CNS system. Thus will be obtained better therapeutic efficiency, minimizing side effects and reducing the frequency of drug administration.

OBJECTIVES

To develop SLN containing DMF and performing physicochemical characterization.

METHODS

The SLN was obtained by ultrasonication method and it was composed by surfactants (poloxamer 188 and soy lecithin), lipid (glycerylmonosterate) and water. Different formulations have been developed by the variation of the lipid contents, surfactants and drug. The SLN were characterized by light scattering (LS), zeta potential (ZP), scanning electronic microscopy (SEM) and atomic force microscopy (AFM).

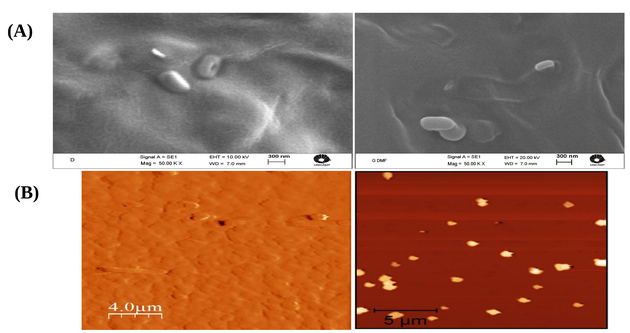
RESULTS

The results showed that the diameter of SLN decreased with increasing the surfactant concentration. On the other hand, the diameter increased with increasing both lipid and drug contents in the formulation. The diameter of DMF-loaded SLN and DMF-unloaded SLN was about 327 and 287 nm, respectively. The ZP was negative in all formulations. By the AFM and SEM images it was possible to identify the morphology of SLN that showed elongated and spherical particles. The AFM and SEM images confirmed the LS results of the SLN diameter.

Table 1 – Diameter and zeta potential of formulations.

Formulations (unloaded)	Diameter (nm)	Zeta potential (mV)	Formulations (loaded with 2%DMF)	Diameter (nm)	Zeta potential (mV)
A (1,5%MG 2%T)	271,5	-16,7	A DMF	298,5	-23,1
B (3%MG 2%T)	254,3	-20,7	B DMF	216,5	-29,2
C (4,5%MG 2%T)	242,2	-26,5	C DMF	275,6	-26,3
D (6%MG 2%T)	515,7	-30,5	D DMF	391,9	-20,1
E (3%MG 1%T)	379,6	-24,1	E DMF	260,3	-22,3
F (3%MG 2%T)	254,3	-20,7	F DMF	216,5	-29,2
G (3%MG 4%T)	229,3	-19,0	G DMF	348,4	-21,3
H (3%MG 6%T)	157,8	-18,9	H DMF	315,4	-18,5

Figure 1 – (A) SEM and (B) AFM images of formulations.



CONCLUSIONS

The SLN described in this study have physico-chemical characteristics that enable them to be used as a carrier for the nasal administration of DMF. Acknowledgements: FAPESP and CNPq for the financial support.