Design and formulation of nano-sized spray dried Efavirenz-Part 1: Influence of formulation parameters

L TSHWEU, L KATATA, S NAIDOO, L KALOMBO, H SWAI
CSIR Material Science and Manufacturing, PO Box 395, Pretoria, South Africa, 0001
Email: ltshweu@csir.co.za – www.csir.co.za

BACKGROUND

Highly active antiretroviral therapy (HAART) has managed to successfully enhance the quality of life for HIV infected patients.

Efavirenz (EFV) is one of the recommended first-line anti-HIV drugs in the WHO guidelines and used mostly in developing countries.

Challenges include:

- Low aqueous solubility (4 μg/ml)
- Low bioavailability (40 – 45%)
- High doses taken daily and side effects

This CSIR project aims to nano-encapsulate an anti-HIV drug into a biodegradable polycaprolactone (PCL) polymer. The nano-encapsulation into polymeric material can protect these drugs from physiological conditions. Controlled and steady drug release can also be achieved as the polymer degrades, resulting in a reduced number of administration schedules, with reduced dosing frequency and increased bio-availability due to the increased surface area of the nano-encapsulated drug.

PROPOSED SOLUTION

In this work, encapsulation of EFV in PCL will be investigated using a scalable spray drying technique and a Taguchi experimental design method to obtain the optimum formulation for preparing nanoparticles.

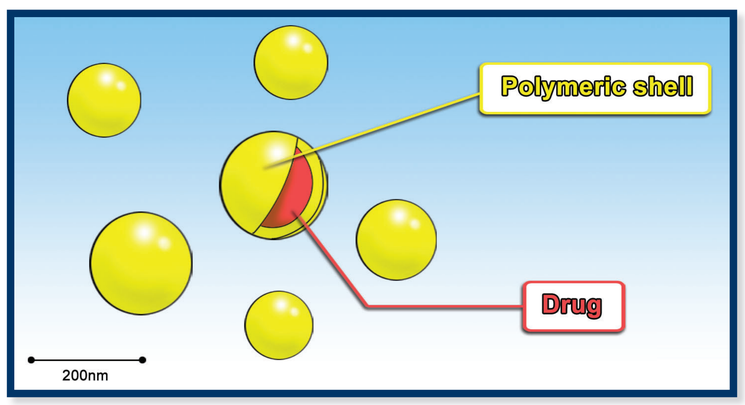

Figure 1: Schematic diagram of polymeric nano-carriers

EXPERIMENTAL DESIGN

In this study, a standard orthogonal array L_8 was used to examine a seven factor system at two levels, as shown in **Table 1**.

Table 1: Taguchi L_8 experimental parameters and levels for preparation of PCL-EFV nanoparticles (NPs)

Symbol	*Formulation parameters*	*Levels*	
		1	*2*
A	W1	PVA	PBS
B	Sugar	Lactose	Trehalose
C	[W2-PVA]	1%	2%
D	[Sugar]	3%	5%
E	Solvent	DCM	EA
F	[W1]	1%	2%
G	[PEG]	0.5%	1%

RESULTS AND DISCUSSION

Organic solvent was the significant parameter that affected particle size and polydispersity index (PDI) on the formulation preparation of the NPs.

The smallest average particle size was found when ethyl acetate (EA) was used as solvent.

The particle size decreased from 689 nm to 237 nm when EA was used compared to dichloromethane (DCM).

OPTIMISED FORMULATION OF PCL-EFV NPs

Predicted optimal conditions resulted in a particle size value of 157 nm, and a PDI value of 0.112. Experimental value yielded average particle size of 217 nm and PDI of 0.09.

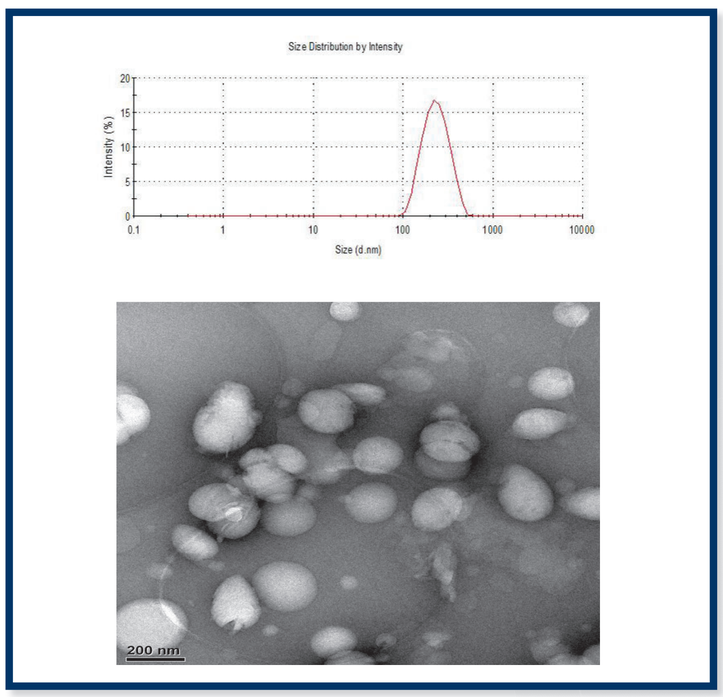

Figure 3: Average S/N ratio for each level of the parameters for particle size of PCL-EFV NPs

SUMMARY AND CONCLUSION

Spherical morphology was observed by TEM analysis.

A Taguchi L_8 method showed to be a fast, simple and valuable tool in optimising the various parameters for the preparation of spray dried PCL-EFV NPs.

The organic solvent was found to be main parameter having significant effects on the particle size and PDI.

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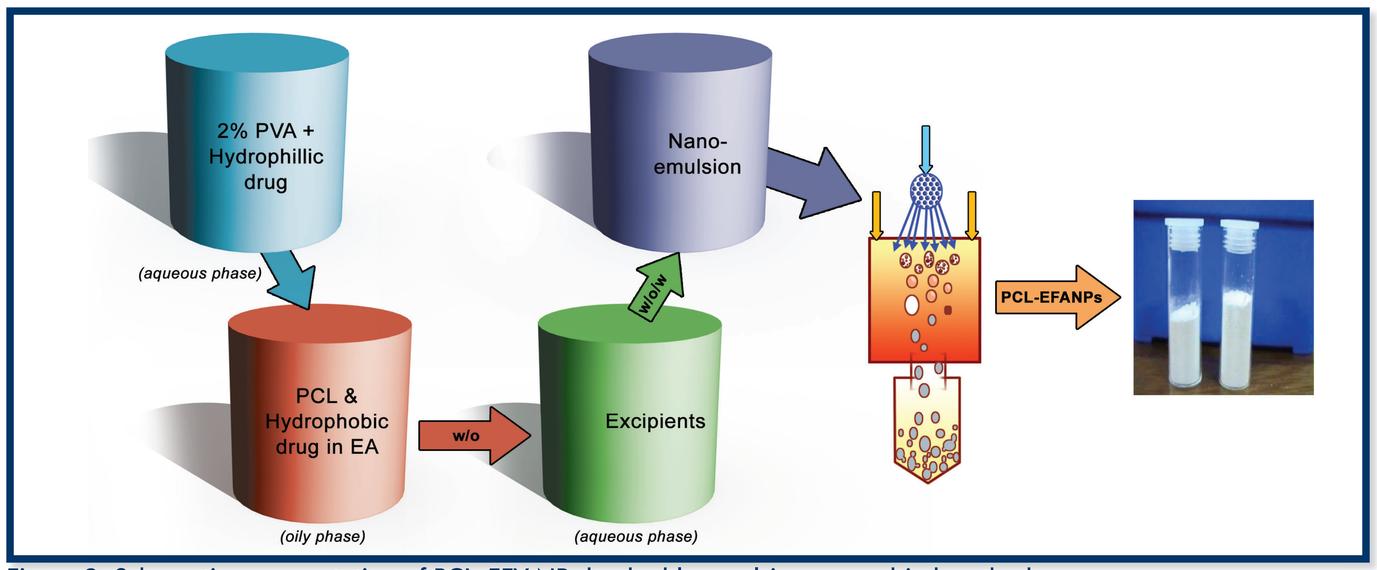

Figure 2: Schematic representation of PCL–EFV NPs by double emulsion spray-dried method

AIDS kills over 1.5 million people a year globally. Current HIV drugs pose many challenges. Research shows that nano-encapsulation of HIV drugs achieves controlled and steady drug release, and reduced dosing frequency.

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