PHARMACOKINETICS OF NIFEDIPINE FORMULATED AS SOLID DISPERSIONS WITH POLYVINYLPYRROLIDONE

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Solid dispersions have proven to be a good strategy to overcome low drug solubility and consequently low dissolution rate and bioavailability. There are already authorized formulations on the market, but the methods of obtaining and the composition of solid dispersions are still being investigated. Industrial applicability and environmental acceptability characterize the supercritical fluid technology (SFT) that could be suitable for formulating solid dispersions.

Previously prepared and characterized nifedipine solid dispersions with polyvinylpriolidone (PVP)

↓ multilevel categorical design

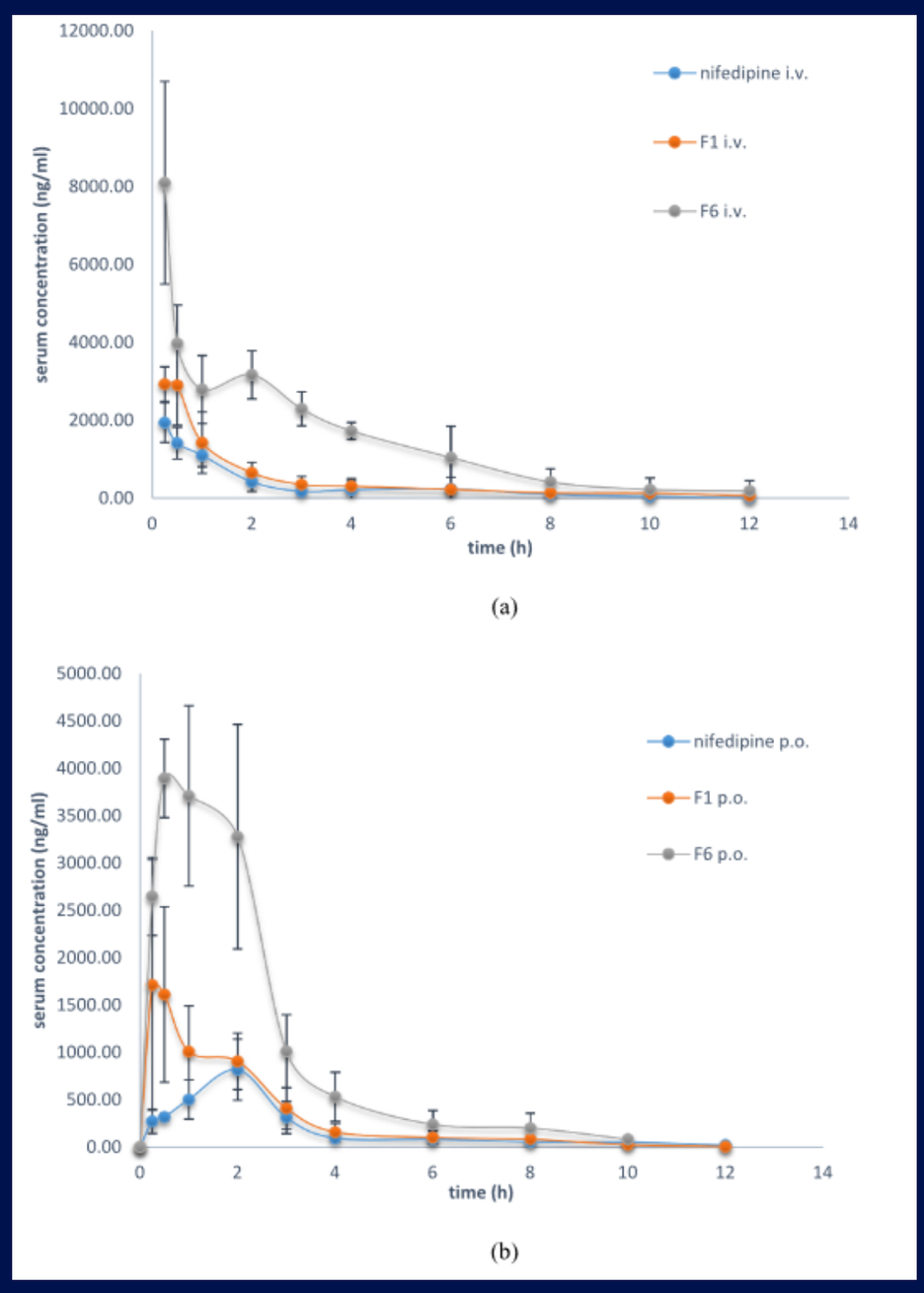
Nifedipine solid dispersion formulations with the best in vitro performances

↓ pharmacokinetics study

Serum concentrations

↓ WinNonlin v. 8.3

Pharmacokinetics parameters



Pharmacokinetic parameters of pure nifedipine and selected formulations (Mean ± SD, n = 6).

pharmacokinetics parameter	nifedipine		F1		F6	
	i.v.	**p.o.**	**i.v.**	**p.o.**	**i.v.**	**p.o.**
λ_z (1/h)	0.26 ± 0.13	0.26 ± 0.13	0.24 ± 0.07	0.44 ± 0.16	0.43 ± 0.18	0.33 ± 0.12
$t_{1/2}$ (h)	3.24 ± 1.43	3.18 ± 1.25	3.05 ± 0.74	1.70 ± 0.43	2.01 ± 1.28	2.36 ± 0.85
AUC_{0-t} (µg/ml*h)	3.52 ± 1.36	2.00 ± 0.35	5.65 ± 1.60	3.76 ± 1.59	17.88 ± 4.73	10.49 ± 1.76
$AUC_{0-\infty}$ (µg/ml*h)	3.83 ± 1.62	2.10 ± 0.34	6.05 ± 1.60	3.81 ± 1.60	18.56 ± 5.49	10.87 ± 1.64
V_z (l/kg)	5.30 ± 2.66	8.86 ± 3.74	3.02 ± 0.90	3.04 ± 1.72	0.63 ± 0.28	1.28 ± 0.51
Cl (l/h/kg)	1.20 ± 0.46	1.95 ± 0.30	0.70 ± 0.16	1.22 ± 0.50	0.23 ± 0.08	0.38 ± 0.06
MRT_{0-t} (h)	1.94 ± 0.66	2.98 ± 0.27	2.12 ± 0.56	2.11 ± 0.46	2.61 ± 0.47	2.20 ± 0.32
t_{max} (h)		2.00 ± 0.00		0.46 ± 0.29		0.88 ± 0.63
C_{max} (µg/ml)		0.78 ± 0.27		1.90 ± 1.24		4.23 ± 0.83
C_0 (µg/ml)	2.47 ± 0.71		4.50 ± 2.54		17.70 ± 8.94	
V_{ss} (l/kg)	3.05 ± 1.28		2.07 ± 0.88		0.67 ± 0.21	

The selection of formulations for the pharmacokinetic study took into account a wider range of in vitro studies results, but the in vivo study showed that the proportion of polymer was crucial for increasing bioavailability. Further optimization of the production process and other pharmaceutical-technological procedures of the F2 formulation would potentially enable obtaining the final product of nifedipine with optimized pharmacokinetics.