Simultaneous determination of lamivudine and zidovudine in fixed dose combinations using near infrared spectroscopy

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Introduction

Simultaneous determination of two or more active components in different pharmaceutical preparations, without previous chemical separation, is a common analytical problem. Published works, such as Brazilian Pharmacopeia, and the United States Pharmacopeia, describe the determination of AZT and 3TC separately, in the raw material or in different pharmaceutical preparations. No published work has been found, however, to describe how this association may be determined in tablets. In the present work, a method using Near Infrared spectroscopy and multivariate calibration was developed for the simultaneous measurement of lamivudine (AZT) and zidovudine (3TC) in fixed dose combinations. The method was applied to determine the content of AZT+3TC in tablets from commercial tablets.

Materials and methods

A particular problem in applying NIR spectroscopy methods in the pharmaceutical industry is the need to include a substantial variability in the calibration set. The content of the active principles or other quality parameter would not vary significantly if the production process were under control. This problem was solved by producing a pilot lot of 33 tablets covering the range of 85 to 115% of industrially-produced tablets, that is 300 mg. for AZT and 150 mg for 3TC. In addition to the pilot lot samples, 78 commercial samples from different lots were collected from separate lots on the production line of the Pharmaceutical Laboratory of the State of Pernambuco (LAFEPE). Of these, 47 were collected at the stage before, and 31 after the coating. To estimate

Table 1. Results for determination of content of AZT and 3TC in tablets using NIR spectroscopy.

Nominal content of active principle	Type tablets to prediction set	PLS Models		Factors	SPA/MLR		Factors*
		RMSEP	*R*		*RMSEP*	*R*	
AZT (300 mg)	Coated	11.5	0.8288	7	14.0	0.8472	24
	Uncoated	11.4	0.7851	5	11.7	0.7954	4
3TC (150 mg)	Coated	3.9	0.8300	7	8.0	0.6032	11
	Uncoated	5.9	0.5273	5	7.9	0.4463	10

*Number of SPA variables.

the content of AZT +3 TC in tablets before and after coating, two types of models were built. The first, for the prediction of the content in uncoated tablets, had 15 uncoated tablets selected using the Kennard-Stone algorithm, in its calibration set, in addition to the 28 tablets produced in the pilot lot. The second model, used to estimate the proportion of coating, had 10 coated tablets, also selected using the Kennard Stone algorithm, and 28 tablets produced in the pilot lot. Thirty-two uncoated tablets, 21 tablets uncoated tablets, and 5 tablets produced in the pilot lot, selected by the Kennard-Stone algorithm, were used in the prediction stage.

The results obtained by the models were compared with those obtained using the official method (HPLC). The spectra of all samples were recorded using a NIR spectrophotometer with Fourier transform, BOMEM, model MB 160, equipped with a *Powder-SamplIR* accessory. All computations were performed using the Unscrambler 9.5 (Camo SA) and Matlab 7.0 (Mathworks) software platforms. Some pre-processing methods were evaluated and the best results were obtained using smoothed spectra (Savitzky-Golay algorithm, second-order polynomial and twenty-one point window). The models were obtained using Partial Least Squares Regression (PLS) and Multiple Linear Regression (MLR). Full cross-validation (*CV*) was employed to select the number of PLS factors and variables (in MLR). The method of variable selection was based the Successive Projections Algorithm (SPA) for the MLR models.

Results and discussion

The results for the models are shown in Table 1.

The predictive ability of the models was evaluated according to the root-mean-square error in the prediction set (*RMSEP*). The results of predictions made using the PLS models for the tablets of AZT, coated or not, have errors in the range of 3.8%. For the 3TC the errors were around 2.6% for coated and 3.9% for the uncoated. The PLS models showed better performance than the MLR. However, the results for both models are within the limits allowed by the pharmacopoeia.

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