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International Journal of Pharmaceutics 177 (1999) 1–6

international journal of pharmaceutics

Qualitative determination of polyvinylpyrrolidone type by near-infrared spectrometry

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Received 5 March 1998; received in revised form 3 July 1998; accepted 30 July 1998

Abstract

Soluble polyvinylpyrrolidones are very useful and versatile pharmaceutical auxiliaries. The different types of povidone are characterised by their viscosity measured in water, expressed as a *K*-value. We have developed a rapid, accurate, reliable, and non-destructive near infrared (NIR) spectroscopy method for the determination of PVP type and consequently identification thereof. We have implemented chemometrics onto NIR spectra collected in diffuse reflectance mode using fibre optics to build a qualitative model that enables us to obtain useful analytical information. A principal component analysis and a modelling technique soft independent modelling of class analogy (SIMCA) were applied. An approach to validate the method was developed.

Keywords: Povidone; Near infrared spectroscopy; Qualitative analysis

1. Introduction

Povidone (polyvinylpyrrolidone, PVP) is poly [1-(2-oxo-1-pyrrolidinyl)ethylene] and consists of linear polymers of 1-vinylpyrrolidin-2-one. The soluble grades of povidone are obtained by free-radical polymerisation of vinylpyrrolidone in water or 2-propanol, yielding the appropriate chain structure (Vieweg et al., 1971; Ullmanns Encyclopaedie der technischen Chemie, 1980). Soluble polyvinylpyrrolidones are very useful and versatile pharmaceutical auxiliaries.

The consequence of regulatory requirements for pharmaceuticals is an identification of all packaging units of raw material delivery. For povidone it would be of great advantage to determine identity and PVP type simultaneously. The different types of povidone are characterised by their viscosity measured in water, expressed as a *K*-value. The *K*-values can be calculated from measured viscosity using the pharmacopoeial method (USP, 1995; The European Pharmacopoeia, 1997).

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0378-5173/99/$ - see front matter
PII S0378-5173(98)00265-8

Thus a rapid, accurate, reliable, and non-destructive method for the determination of PVP type and consequently identification thereof, would be of great importance. The near infrared (NIR) spectroscopy has been used for qualitative and quantitative analysis, e.g. identity, determination of raw materials and dosage forms, quantitative determinations in different pharmaceutical dosage forms (Plugge and Van der Vlies, 1992; Dempster et al., 1993; Jones et al., 1993; MacDonald and Prebble, 1993). The use of NIR in powder-mixing studies has also been reported (Ciurczak, 1991).

NIR diffuse reflectance techniques have important advantage for the direct analysis of solids without the necessity for sample preparation (Buback, 1995). An additional benefit is conformity testing of material being determined, then releasing it for the use without additional laboratory testing. NIR spectrometry is a technique particularly useful for identifying organic substances. NIR spectra show that even large molecules exhibit only relatively few bands. The spectra are restricted to C–H, N–H, O–H, and S–H resonances, which appear as lower overtones and lower order combination modes. Thus, NIR spectroscopy is less suitable for direct detailed qualitative analysis than IR spectroscopy, although the implementation of chemometrics with NIR spectra allow the building of different models (e.g. a qualitative model) which enables useful analytical information to be obtained.

The model validation is the last step in its generation. The objective of a model validation is to demonstrate that it is suitable for its intended purpose, e.g. the determination of different PVP types simultaneously with the conformity test. The application of conformity testing should detect abnormal material. Thus, the selection of the proper validation procedure is very important to verify conformance specificity.

2. Materials and methods

2.1. Samples

The samples of three different types of polyvinylpyrrolidone (Povidone, BASF) have been included in this study: K 25, K 30, and K 90 F. The samples were divided into calibration and test (prediction) sets randomly, although for the prediction set the samples with extreme *K*-value were omitted. The samples of another two types of PVP (i.e. K 12PF, and K 17PF, respectively) were used in the model validation.

2.2. Methods

The primary reference data were generated with the determination of the relative viscosity and then the *K*-value was calculated from the relative viscosity (USP, 1995; The European Pharmacopoeia, 1997). Kinematic viscosities of 1% w/w solutions of polyvinylpyrrolidone were measured using a Ubbelohde viscosimeter (Schoot).

NIR spectra were collected in triplicate using a Fourier-transform NIR spectrometer (InfraProver II, Bran and Luebbe, Germany). The spectra were collected in the wavelength range from 4500 to 10000 cm^{-1} in diffuse reflectance mode using fibre optics at a resolution of 25 cm^{-1}, and afterwards converted to absorbance with a log(1/R) transformation.

Table 1
The number of samples used for the model generation and their corresponding *K*-values

Type	Set	No. of samples	*K*-value range	Ph. Eur., USP limits for *K*-value
K 25	Calibration	49	24.9–26.4	22.5–27.0
	Prediction	23	25.4–25.9	
K 30	Calibration	26	29.5–31.4	27.0–32.4
	Prediction	13	30.2–31.1	
K 90 F	Calibration	15	87.3–93.9	81.0–97.2
	Prediction	12	87.5–89.7	

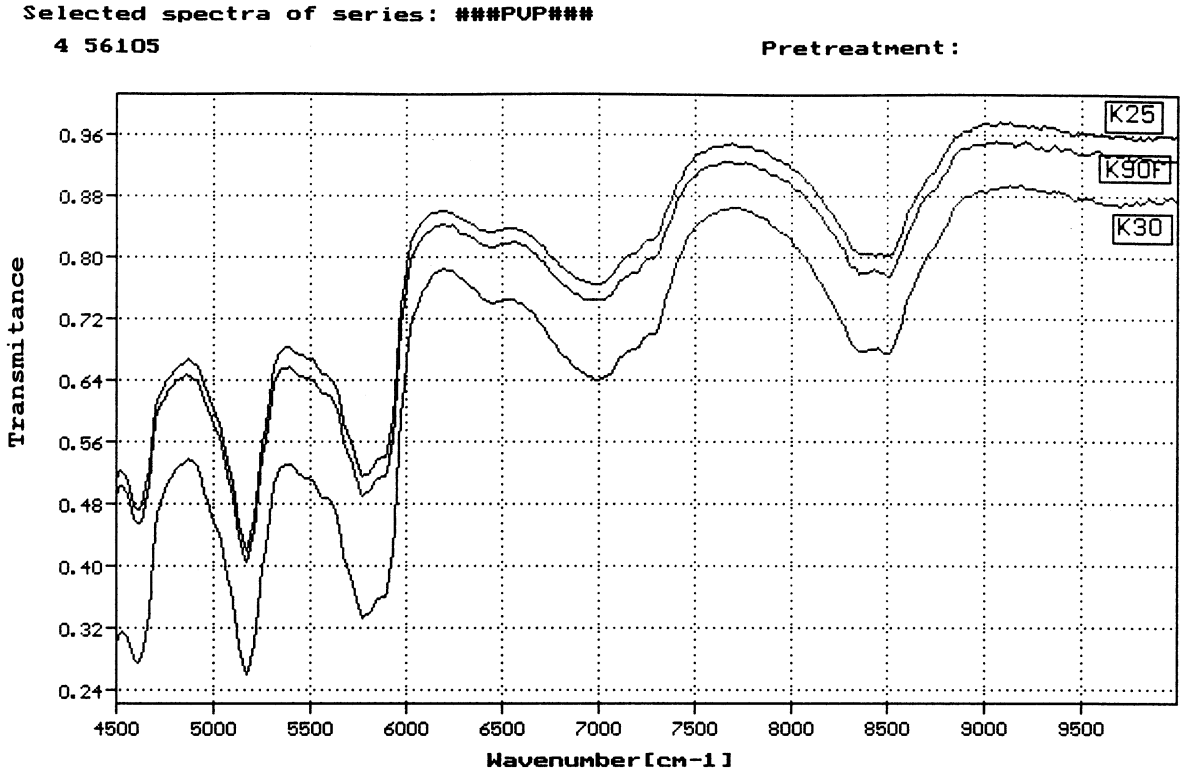

Fig. 1. FT-NIR spectra (top-to-bottom): PVP K 25, PVP K 90 F, and PVP K 30.

A principal component analysis (PCA) (Massart et al., 1988a; Cowe et al., 1990) and soft independent modelling of class analogy (SIMCA) (Massart et al., 1988b) were performed utilising the whole spectral range.

3. Results and discussion

In Table 1 the number of samples used for the model generation and their corresponding *K*-values are presented.

FT-NIR spectra (Fig. 1) of three different types of povidone are presented. The determination of the PVP type from the NIR spectra themselves is not possible, as the spectra do not differ from each other because of the same functional groups in polymers as shown in Fig. 1.

However, the application of chemometric analysis on NIR spectra allows the resolution of different PVP types using principal component analysis and a modelling technique SIMCA (Massart et al., 1988a,b).

In modelling the original NIR spectra were used. The spectra were transferred into the factor space, where each point corresponds to an individual spectrum. The number of principal components describing systematic variations was determined. As the systematic variations are described by the relevant principal components we investigated the behaviour of the loadings of the samples with respect to these principal components. If there is a correlation of a principal component to the class properties we expected the loadings of the samples belonging to the same class to be close together in the topological sense. We were looking for the relevant principal components using the correlation indexes equal to the number of class changes that occur. If the clustering occurs in the selected principal component, there should be relatively few class changes and the correlation index should be small in its abso-

lute value. After investigating the principal components with the lowest correlation indexes, two principal components were chosen with respect to the best clustering. Using correlation indexes of component loadings and two-dimensional representation of factor space, two components were selected for a model able to separate individual types of PVP spectra. With appropriate components, similar spectra should be grouped into corresponding connected clusters that should be clearly separated from each other. Thus, it is important that the differences between spectra of different types of PVP are big enough, in contrast to the differences between spectra of different samples within one type of PVP. Grouping into the clusters is represented in Fig. 2.

The factor space defined by the selected components has been divided into regions associated with each class by surrounding each sample with the sphere of half the radius to the closest sample of another class.

The final step in model generation is its validation. A three step validation was performed. The first step determines whether the algorithm is capable of distinguishing between each product in the model. Each spectrum used in the model development was tested.

Around each class virtual points are defined by constructing the smallest hypercube in the space of loadings of the selected components that completely contains all samples of the class.

For each sample of the class the minimum distance between all samples belonging to any other class and all virtual points belonging to the class is calculated. The maximum allowed residual has been calculated from residuals over the whole calibration set. The residual of an unknown sample must be within determined residual limits, otherwise it has to be rejected.

In the second step the ability of the model to recognise the samples was accomplished using the test sample set. The accuracy of the NIR method

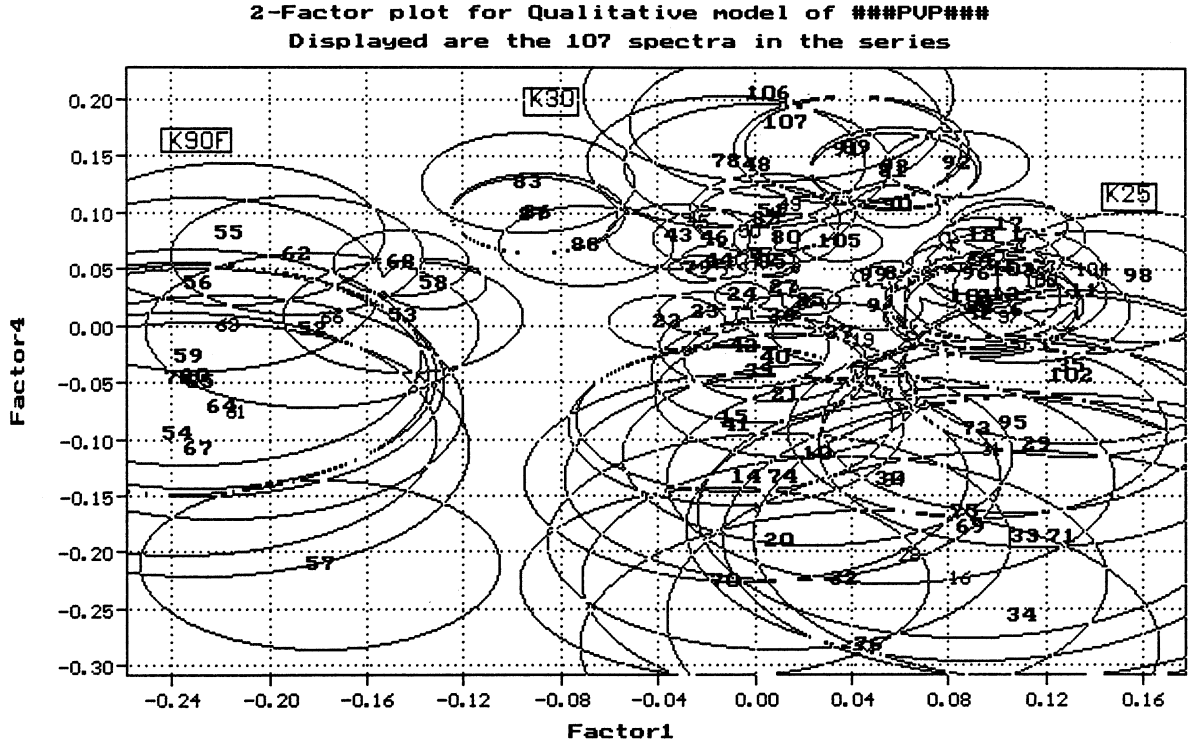

Fig. 2. Grouping of NIR data of PVP K 25, PVP K 30, and PVP K 90 F into the clusters is possible with appropriate components chosen.

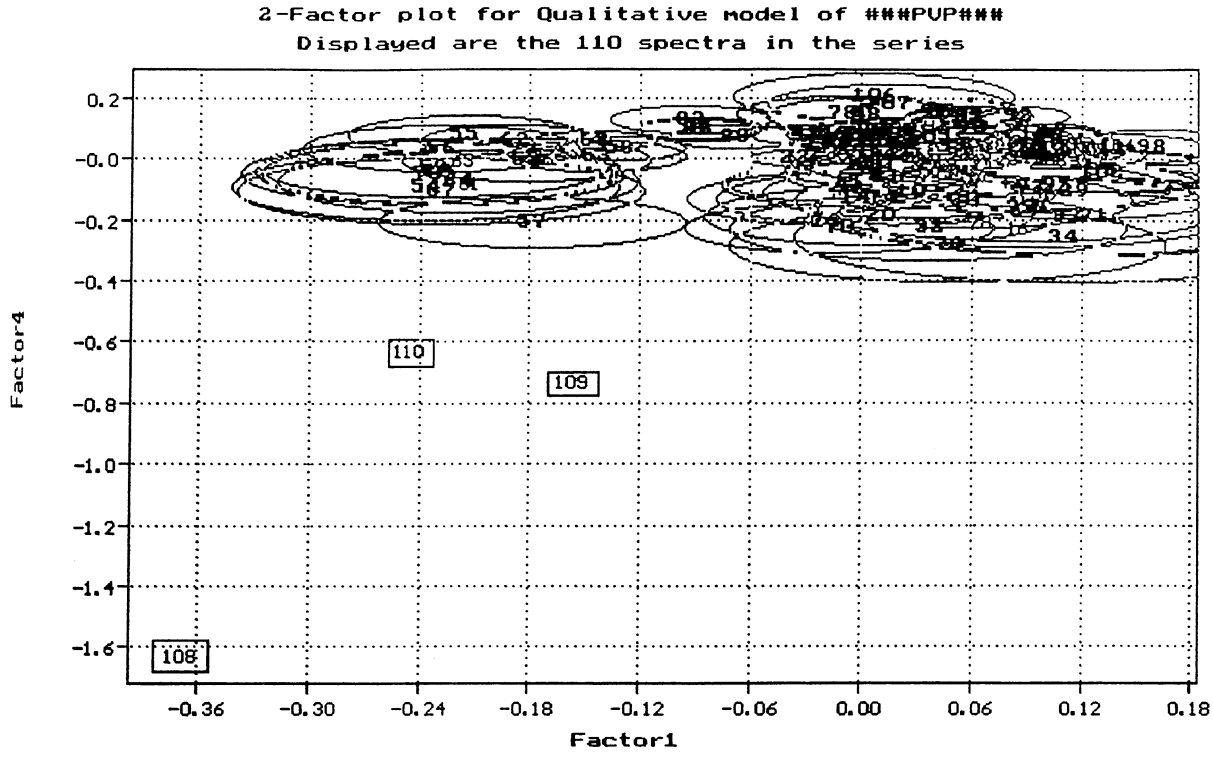

Fig. 3. Samples of other PVP types were not recognised as correct by the model; (108), PVP K 12PF; *K*-value, 10.2–13.8; (109) and (110), PVP K 17PF; *K*-value, 15.3–18.0.

was first checked with samples that were within all the pharmacopoeial specification limits (conformable samples). All conformable test samples were identified correctly (Table 1).

In continuation, we have also tested the samples where the water content exceeded the specification limits, and also the viscosity of these samples was not within the calibration set range (unconformable samples). None of the unconformable samples was recognised as correct by the model. The validation of method specificity was performed using samples from other PVP types of the same supplier (Section 2), and they were not recognised as correct samples by the model (Fig. 3).

The last validation step was the cross-validation. It was performed with spectra of all substances in the database. Except spectra of the products in the model no other spectra have been correctly identified within the model. We checked the majority of the substances supplied to the factory, including insoluble grades of PVP.

The developed NIR method is except for the determination of sample identity appropriate also for qualitative testing.

4. Conclusions

The identification of pharmaceutical raw materials (e.g. povidone) by the NIR method offers an advantage of being less time consuming, ecologically acceptable, and more cost-effective in comparison to indirect method (e.g. using the determination of the *K*-value by viscosity measurement for PVP type). An additional benefit is simplicity of analysis.

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