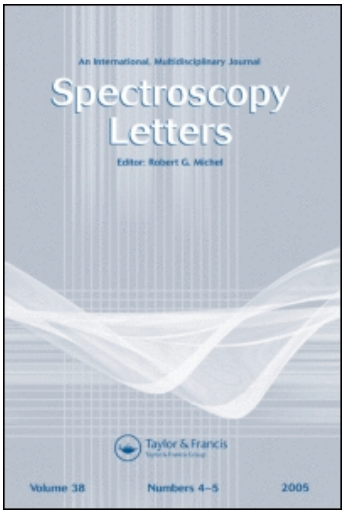

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Quality Control of Pharmaceutical Aspirin Powder by Near-Infrared Reflectance Spectra and Multivariate Analysis

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QUALITY CONTROL OF PHARMACEUTICAL ASPIRIN POWDER BY NEAR-INFRARED REFLECTANCE SPECTRA AND MULTIVARIATE ANALYSIS

Key Words: Near infrared spectrometry, diffuse reflectance, multivariate analysis, quality control, acetyl salicylic acid

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ABSTRACT

Quality control of pharmaceutical aspirin powder was studied using first order differential near-infrared diffuse reflectance spectra and four standard multivariate methods, hierarchical clustering analysis, stepwise clustering analysis, principal components analysis, and stepwise discrimination. The qualified, inferior, and fake pharmaceutical aspirin powders of independent samples can be distinguished by the multivariate analysis methods based on the reflectance spectra. The proposed methods are reliable, fast and nondestructive.

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INTRODUCTION

Near-infrared (IR) reflectance spectrometry is being applied as a fast, nondestructive analytical method in analysis of various kinds of biomedical and pharmaceutical compounds. The quality control of pharmaceuticals is becoming more rigid by government regulations and clinic standards. The qualitative classification and quantitative analysis of pharmaceuticals in production and sales procedures are required , especially for nondestructive identification and analysis. Ciurzak[1] reviewed the application of near-IR to pharmaceutical analysis. Recently, Kirsch and Drennen[2] reviewed the application of near-IR in the analysis of tablets and solid pharmaceutical dosage forms. Various near-IR techniques including diffuse reflectance have been used in the identification, quantitative, and quality control[3-10].

The application of near-IR spectrometry to pharmaceuticals of various solid dosage formulations is a significant advance in pharmaceutical analysis because it explored the potential of the method for more pharmaceutical processes. The practical application of near-IR is based on the computer techniques and chemometric method to a large extent. In most cases, in fact, the use of chemometric methods is necessary because of numerous overlapped absorption bands exist in the near-IR region[3].

Four standard multivariate methods, hierarchical clustering analysis, stepwise clustering analysis, principal component analysis, stepwise discrimination, were used for the study on quality control of pharmaceutical aspirin powder using differential near–IR diffuse reflectance spectra. Results show that the different qualities of samples, qualified, inferior, and fake aspirin medical powders, can be distinguished correctly. Satisfactory results were obtained.

EXPERIMENTAL

A Shimadzu® UV–3100 spectrometer with an ISR–3100 integrating sphere was used for the near–IR diffuse reflectance spectra measurement. Data were transferred to a microcomputer through a RS–232C interface. A Pentinium–based microcomputer was used for data processing and computation.

The aspirin (acetyl salicylic acid), starch and talcum powder were used according to the pharmacopoeia.

Forty-three pharmaceutical aspirin powder samples were prepared according to the prescription. These samples were divided into two groups: the training set and the prediction set. Of which thirty-one samples were qualified with required amount of aspirin (from number 1 to 23 in training set and from 33* to 40* in prediction set) and seven inferior samples (24–28 in training set and 41* and 42* in prediction set). Five samples, numbered 29–32 in training set and number 43* in prediction set, were fake aspirin powder samples which did not contain the aspirin at all. The contents of every components in the aspirin medical powders are given in TABLE 1.

The entrance slit of the near-IR spectrophotometer used was 12 nm and the scan wavelength range was from 1100 to 2500 nm. Two repeated spectral scans were made and all the spectra were average of the two. Eighty-one data points (absorbances) for each spectrum were used.

RESULTS AND DISCUSSION

The conventional near–IR reflectance spectra of pure acetylsalicylic acid, starch and talcum powder and the first order differential reflectance spectra are shown in FIG.1 (a) and (b), respectively. Serious overlaps of the absorption bands can be seen from the FIG. 1 (a), whereas, the resolution was enhanced by using the first order differential spectra, as shown in the FIG. 1 (b). For this reason, the differential spectra were used for the statistical multivariate analysis. Higher order differential spectra would result in high level of noise.

Hierarchical Clustering Analysis

The hierarchical clustering analysis (HCA) is based on the idea that "similar things gather together". According to a given criterion of similarity or dissimilarity (distance), the samples were classified into some clusters in a multi-dimensional space. The classification can be easily drawn using a dendrogram.

Dendrograms of training set and all prepared samples, respectively, using Euclidean distance and the Ward method for first order differential near-IR reflectance spectra is shown in FIG. 2. It can be seen from the FIG. 2 (a) that the fake aspirin powder samples (sample numbers 29–32) are

TABLE 1. Component Contents of the Aspirin Powders (%, w/w)

Quality	Acetylsalicylic acid			Starch			Talcum powder		
	max.	min.	mean	max.	min.	mean	max.	min.	mean
Qualified (31)	88.84	80.64	84.56	13.84	6.62	10.79	5.06	4.41	4.72
Inferior (7)	76.12	42.68	63.87	51.43	19.10	31.37	5.87	4.04	4.78
Fake (5)	0	0	0	95.66	95.39	95.52	4.61	4.34	4.45

obviously separated from others. The qualified and inferior aspirin powder samples can also be distinguished clearly. To test the prediction ability of the method, some independent prediction samples were added to the original training samples together and were calculated again. The dendrogram with independent prediction samples is given in FIG. 2 (b). The qualified aspirin samples (numbers 33*–40*), inferior samples (numbers 41* and 42*), and fake aspirin powder (number 43*) fell into right clusters, respectively, as shown in the dendrogram of FIG 2(b).

Stepwise Clustering Analysis

Stepwise cluster analysis (also called dynamic cluster analysis) is an iterative method which based on the centroids of clusters in multi-dimensional space. The distance of each object to each centroid is adjusted in each step until the distances keep unchanged. Three centroids based on the first order differential near infrared reflectance spectra of training samples were obtained and the distances of each sample to each centroid were calculated. All the samples can be clustered according to the distances. The distances of training samples are shown in FIG. 3 (a) and the distances of all samples including training and independent prediction samples are shown in FIG. 3 (b). The distances of prediction samples to each centroid are given in TABLE 2. Samples with smaller distances to a centroid fell into the corresponding cluster. It can be seen that all the independent testing samples are classified to right clusters, respectively.

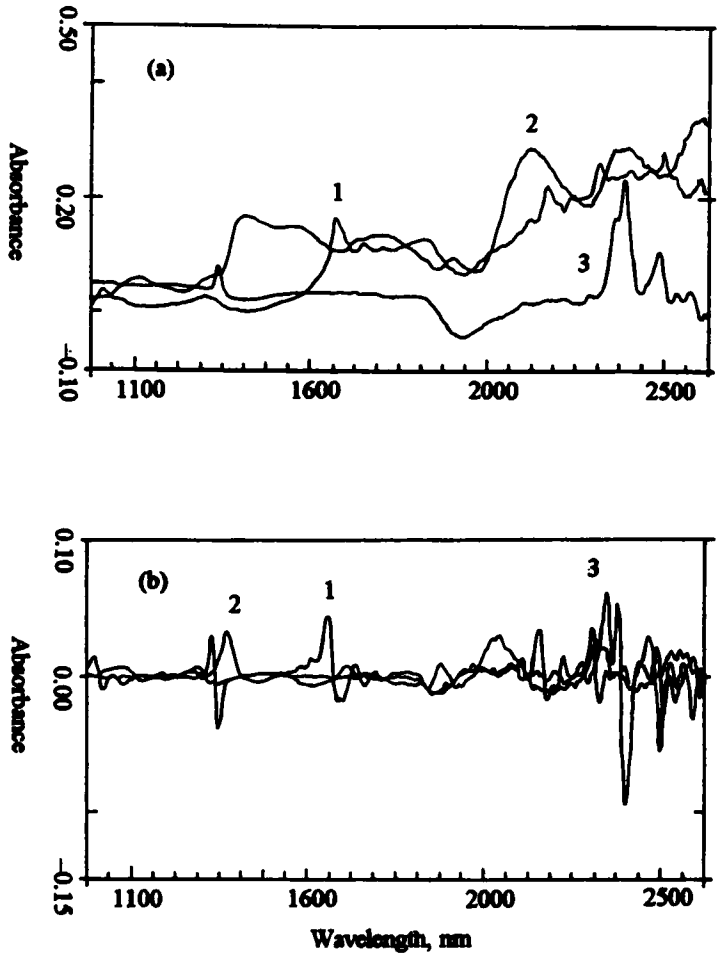

FIG 1. Near infrared reflectance spectra of the typical aspirin powder
(A) Conventional spectra; (B) First order differential spectra.
Curve 1: Acetylsalicylic acid; curve 2: Starch; curve 3: Talcum powder

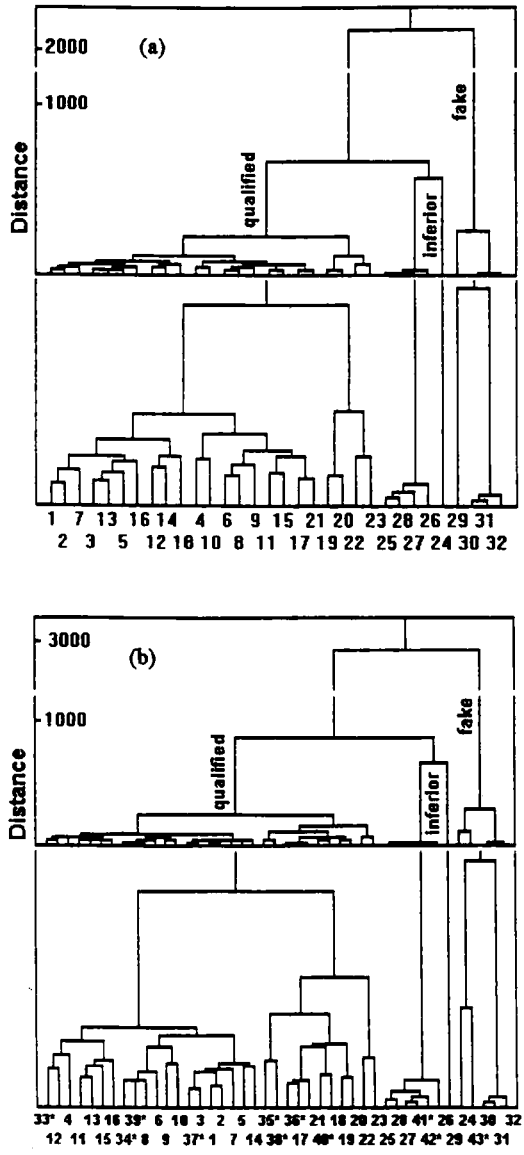

FIG 2. Dendrograms for pharmaceutical aspirin powders
(A) Training set; (B) Training set and prediction set together

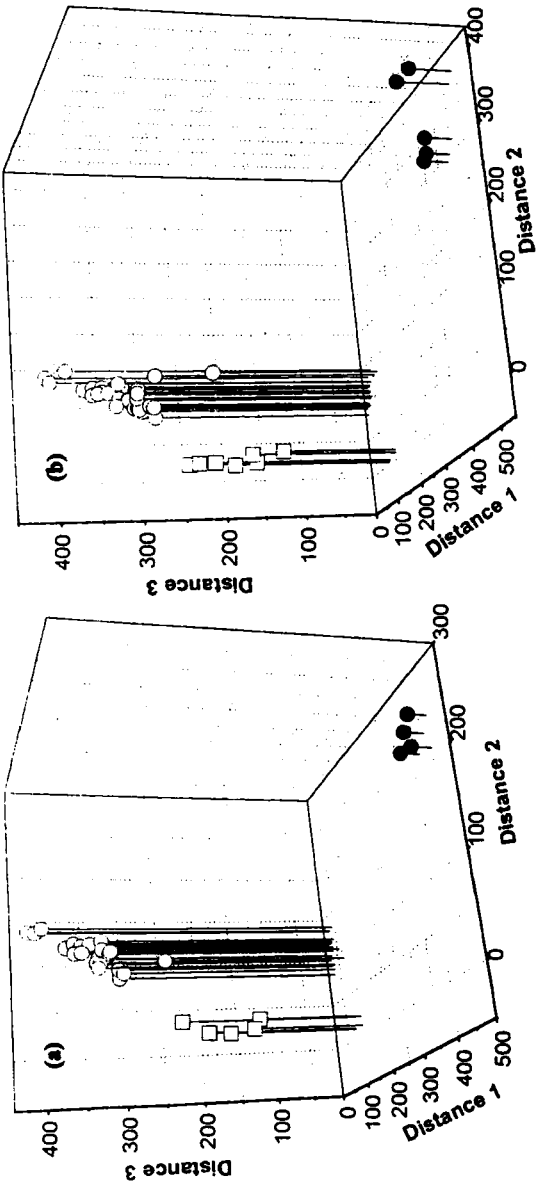

FIG 3. Graphical presentation of the stepwise clustering analysis results (A) Training set; (B) Training and prediction sets together

TABLE 2. Results of Prediction Samples by Stepwise Clustering Analysis

No.	dist. 1	dist.2	dist. 3	Judge✞
33*	33.58	112.07	341.08	Q
34*	15.35	82.91	282.72	Q
35*	40.32	103.16	307.81	Q
36*	19.60	105.99	313.96	Q
37*	14.03	91.94	297.16	Q
38*	35.73	110.62	305.83	Q
39*	21.35	95.20	304.29	Q
40*	24.99	93.89	309.02	Q
41*	84.93	5.84	247.27	I
42*	81.90	6.94	247.55	I
43*	473.49	381.44	72.69	F

✞ The symbols Q, I and F denote qualified, inferior, and fake aspirin powders, respectively.

TABLE 3. Results of PCA for Aspirin Powder

	Var 1	Var 2	Var 3	Var 4	Var 5
eigenvalue	41.76	11.51	6.52	3.95	2.60
prop.	0.52	0.14	0.08	0.05	0.03
cum. prop.	0.52	0.66	0.73	0.79	0.82

Principal Components Analysis

Principal components analysis is a data compression methods. It extracts main factors from complex data while remaining the most significant information as possible.

The eigenvalues of first five principal components based on the first order differential near-IR reflectance spectra are given in TABLE 3. The training samples based on the first three principal components are shown in FIG. 4

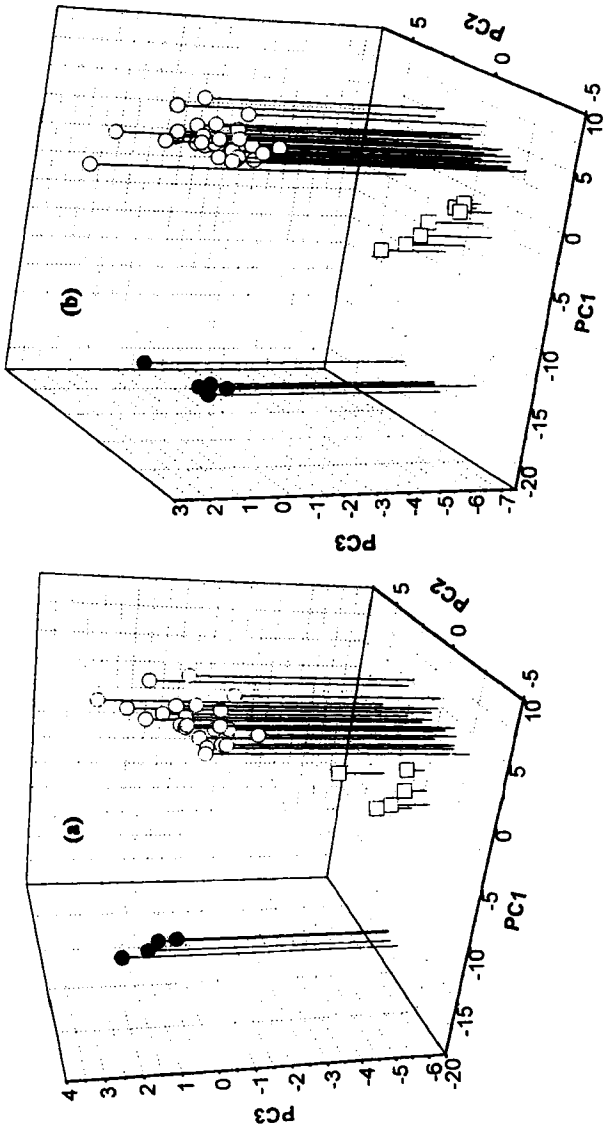

FIG 4. Graphical presentation of the principal components analysis results (A) Training set; (B) Training and prediction sets together

TABLE 4. Results of Prediction Samples by Stepwise Discrimination

No.	Y 1	Y 2	Y 3	Judge†
33*	187.64	140.20	−145.21	Q
34*	236.82	166.97	−153.78	Q
35*	207.63	151.01	−142.72	Q
36*	296.91	198.88	−173.84	Q
37*	216.50	155.50	−151.43	Q
38*	230.90	159.90	−147.42	Q
39*	257.82	182.60	−165.26	Q
40*	227.73	158.48	−144.03	Q
41*	57.97	112.02	−141.40	I
42*	−1.80	73.49	−118.04	I
43*	−334.71	−128.99	−2.99	F

† The Q, I and F denote qualified, inferior and fake aspirin powders, respectively.

(a). The training samples together with independent prediction samples based on the first three principal components are shown in FIG. 4 (b). It can be seen that the qualified, inferior, and fake samples can be classified correctly using the PCA, especially in three dimensional display.

Stepwise Discrimination

This method is based on linear discrimination model and based on the F test. Significance was tested based on F test in each step and non-significant variables was excluded until the most information was kept with minimum variables. Discrimination functions can be obtained and these functions can be used for the classification. The discrimination functions obtained for this example are given as following, in which F east level of 4.5 was used.

$$Y_1 = -232.27 - 6312.64x_{1315} - 10314.55x_{1915} + 15881.10x_{2035} - 9059.50x_{2125} + 3910.42x_{2155}$$

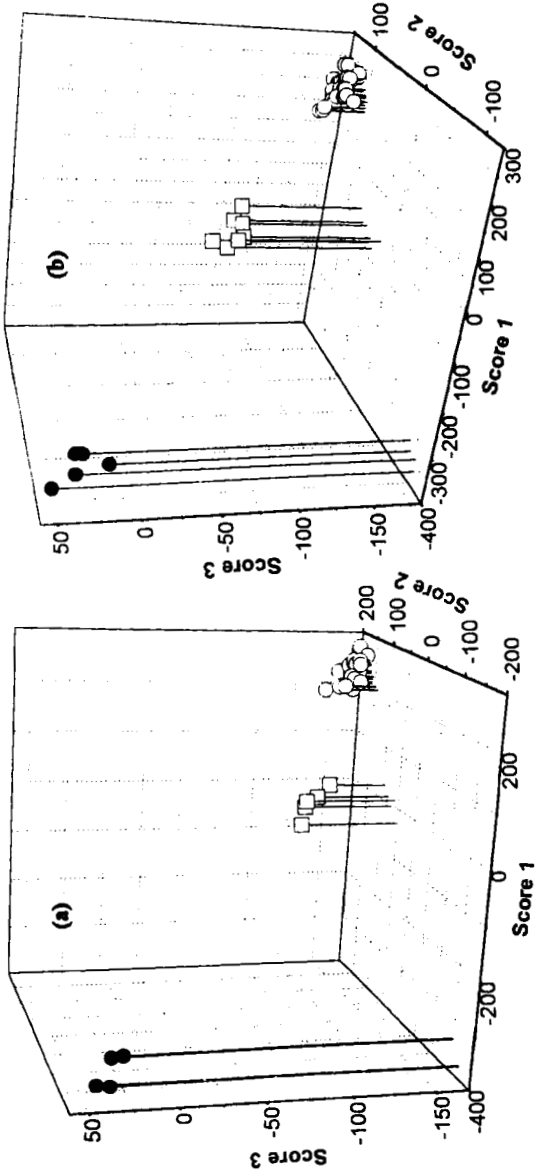

FIG 5. Graphical presentation of stepwise discrimination results
(A) Training set; (B) Training and prediction sets together

$$Y_2 = -72.68 - 3794.57x_{1315} - 5226.29x_{1915} + 10636.79x_{2035} - 8264.92x_{2125} + 509.29x_{2155}$$

$$Y_3 = -32.103 + 1949.96x_{1315} + 5226.29x_{1915} - 10726.52x_{2035} + 5711.92x_{2125} + 462.21x_{2155}$$

where x_i is variable corresponding to the differential spectral peak in differential spectra, and the subscript denotes the wavelength selected. The five variables are corresponding to component peaks aspirin at 2155 nm and 2125 nm, starch at 1915 nm and 2035 nm, and talcum powder at 1315 nm, respectively.

The discrimination results obtained for independent prediction samples based on differential near infrared reflectance spectra are given in TABLE 4.

When the Y_1 is the largest value, is sample is qualified, when Y_2 is the largest value, the sample is inferior, and when the Y_3 is the largest, the sample is fake. All independent prediction samples were classified by the discrimination functions. All samples including training and independent prediction samples presented in three dimensional graph are shown in FIG. 5.

It can be seen that the stepwise discrimination is more straightforward comparing to the three methods discussed previously because the problem discussed was linearly discriminated.

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REFERENCES

1. Ciurzak E W. Uses of Near-infrered Spectroscopy in Pharmaceutical Analysis. Appl. Spectrosc. Review 1987; 23(1):147.
2. Kirsch J D., Drennen J K. Near-infrared Spectroscopy: Application in the Analysis of Tablets and Solid Pharmaceutical Dosage Forms. Appl. Spectrosc. Review 1995; 30(3):139.
3. Donald A B., Emil W C. Handbook of Near-infrared Analysis, New York: Marcel Dekker, Inc., 1992.

4. Dressi E., Ceramelli G., Corei P. Near-infrared Reflectance Spectrometry in the Determination of the Physical State of Primary Materials in Pharmaceutical Production. Analyst 1995; 120:1005.
5. Dempster M A ., McDonald B F., Gemperline P J., Boyer N R. Near-infrared Reflectance Analysis Method for the Noninvasive Identification of Film-coated, and Blister-packed Tablets. Anal. Chim. Acta 1995; 310:43.
6. Corti P., Dreassi E., Corbini G., Ballerini R., Gravina S. Application of Reflectance NIRS Spectroscopy to Pharmaceutical Quality Control Solid Binary Mixtures. Pharm. Acta Hel 1990; 65:189.
7. Corti P., Dreassi E., Ceramelli G., Lonardi S., Viviani R., Gravina S. Near Infrared Reflectance Spectroscopy Applied to Pharmaceutical Quality Control, Identification and Assay of Cephalosporins. Analusis 1991; 19:198.
8. Corti P., Savini L., Dreassi E., Ceramelli G., Montecchi L., Lonardi S. Application of NIRS to the Control of Pharmaceuticals Identification and Assay of Several Primary Materials. Pharm. Acta Hel 1992; 67(2):57.
9. Corti P., Dreassi E., Murrantzu C., Corbini G., Ballerini L., Gravina S. Application of NIRS to the Quality Control of Pharmaceuticals Ketoprofen Assay in Different Pharmaceutical Formulae. Pharm. Acta Hel 1989; 64(5-6):140.
10. Dreassi E., Ceramelli G., Corti P., Lonardi S., Perruccio P L. Near-infrared Reflectance Spectrometry in the Determination of the Physical State of Primary Materials in Pharmaceutical Production. Analyst 1995; 120:1005.

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