Original Article

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A novel classification method for determination of Sertraline in pharmaceutical formulation containing different amount of excipients

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Abstract

Attenuate Total Reflectance Infrared Spectroscopy (ATR-IR) method is a routine, easy and non-time consuming approach to determine and detect drugs in pharmaceutical samples. In this study, sertraline as a widely used antidepressant drug was mixed with various amounts of tablet matrix excipients (lactose, starch and sodium lauryl sulfate that are common excipients in tablet formulations) and the amount of sertraline was assessed by ATR-IR method. At first, ATR-IR spectra data converted to normal matrix by SNV preprocessing approach and then, related signals were assessed by chemometrics model (Partial least Partial Least Squares Discriminant Analysis (PLS-DA)) with different variables. PLS-DA is able to analyze highly noisy ATR-IR data and can provide a variety of useful and accurate statistics and predictions. The model was able to determine sertraline amount in précised approach with zero error percentage when the number of the components was 7. As a result, the method was able to predict the sertraline amount and can be used in other applications of drug quantitation.

Keywords: ATR-IR, Chemometrics, PLSDA, Sertraline

1. Introduction

Sertraline, [(1S,4S)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthyl(methyl)- amine] is a member of selective serotonin reuptake inhibitors (SSRIs) drugs. It is known as Zoloft or Asentra and potentially inhibits serotonin reuptake into presynaptic nerve fibers in central nervous system (1). It is mostly prescribed to treat depression, obsessive-compulsive disorder, panic disorder and social anxiety disorders. In 2013, it was reported that sertraline was the most prescribed antidepressant agent on the United States market (2).

Many analytical methods have been reported for detection and quantitation of sertraline in different pharmaceutical and biological samples including high-performance liquid chromatography (HPLC), HPLC mass spectrometry (HPLC–MS-MS), capillary electrophoresis and gas chromatography–mass spectrometry (GC–MS). All mentioned methods are accurate and precise in drug detection and determination, however, they are expensive and time-consuming, and need massive sample preparation and different organic and inorganic solvents (3, 4).

ATR (Attenuate Total Reflectance) Mid-infrared (MIR) spectroscopy is known as a non-interfering and simplistic technique in drug analysis and controls (5-7). This method has various advantages such as rapid performance, no need for time-consuming and complex sample preparations and ability to detect special ingredient among oth-

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er components (8-10).

One important point in ATR analysis is that the output data from MIR spectra cannot be directly interpreted because of huge volume of unintelligible chemical peak specificity. As a result, chemometric tools are needed to process data (11).

In this paper, a ATR method was developed to provide a quantitative method for sertraline detection in combination with different excipients and perform a proper chemometrics modeling (Partial Least Squares Discriminant Analysis (PLS-DA)) that can interpret the analysis in the best way (12, 13). PLS-DA is used whenever response variable is categorical. In another meaning, it is a dimensionality reduction method which compromise between the usual discriminant analysis on the principal components of the predictor variables. PLS-DA discovers a linear regression model by ordering the predicted variables and the observed variables into a new space (14, 15).

2. Materials and methods

2.1. Material

Sertraline was purchased from Alborz Co., Iran. Lactose monohydrate, starch and sodium lauryl sulfate (SLS) were purchased from Merck, Germany.

2.2 Preparation of sample mixtures

Different percentages of sertraline as active pharmaceutical excipient was mixed with different amounts of starch, lactose and SLS as the most common excipients used in pharmaceutical tablet formulations as the main market dosage form of sertraline.

Table 1 shows all mixtures prepared for

Table 1. Percentage of different excipients in formulation mixtures.

Sertraline	Starch	Lactose	SLS	Sertraline	Starch	Lactose	SLS
0	49.5	49.5	1	25	37	37	1
0	49	49	2	25	36.5	36.5	2
0	48.5	48.5	3	25	36	36	3
0	39.5	59.5	1	25	29.6	44.4	1
0	39	59	2	25	29.1	43.9	2
0	38.5	58.5	3	25	28.6	43.4	3
0	59.5	39.5	1	25	44.4	29.6	1
0	59	39	2	25	43.9	29.1	2
0	58.5	38.5	3	25	43.4	28.6	3
12.5	43.25	43.25	1	37.5	30.75	30.75	1
12.5	42.75	42.75	2	37.5	30.25	30.25	2
12.5	42.25	42.25	3	37.5	29.75	29.75	3
12.5	34.6	51.9	1	37.5	24.6	36.9	1
12.5	34.1	51.4	2	37.5	24.1	36.4	2
12.5	33.6	50.9	3	37.5	23.6	35.9	3
12.5	51.9	34.6	1	37.5	36.9	24.6	1
12.5	51.4	34.1	2	37.5	36.4	24.1	2
12.5	50.9	33.6	3	37.5	35.9	23.6	3
17.5	40.75	40.75	1	50	24.5	24.5	1
17.5	40.25	40.25	2	50	24	24	2
17.5	39.75	39.75	3	50	23.5	23.5	3
17.5	32.6	48.9	1	50	19.6	29.4	1
17.5	32.1	48.4	2	50	19.1	28.9	2
17.5	31.6	47.9	3	50	18.6	28.4	3
17.5	48.9	32.6	1	50	29.4	19.6	1
17.5	48.4	32.1	2	50	28.9	19.1	2
17.5	47.9	31.6	3	50	28.4	18.6	3

ATR analysis. 54 mixture formulations were prepared in water and each formula was analyzed three times by Vertex 70 FT-IR spectrometer (Vertex 70, Germany) at room temperature. Spectra recorded between 4000 cm^{-1} and 1100 cm^{-1} with nominal resolution 4 cm^{-1} with 128 co-added scans. Before collecting sample mixtures spectra data, distilled water was used as reference for background correcting. Sample formulations were dropped on attenuated total reflection (ATR) cell that was equipped with a diamond crystal prism.

2.3. Chemometric data analysis Software

Modeling calculations were functioned on a Core i5 (Intel) laptop running on windows operating system. Matlab® software (Mathworks Inc., Natick, MA, USA) with SVM Toolbox (Eigenvesctor Research Inc., version R2012a) was applied for spectra data analysis. Other manipulations operated with own codes written in Matlab® software package.

2.4. Chemometrics model proportion and data separation

The ATR-IR spectra were processed by standard normal variate (SNV) method to enhance resolution of overlapping bands and reduce baseline offsets.

In the next step, ATR-IR outputs were separated into (training) and validation (test) sets by applying Kennard-stone algorithm which is based on Euclidean distance of data set. In other meaning; the algorithm begins with selection of first two objects that have maximum distance from each other. Next object is chosen to have the farthest distance from the primarily selected set and this process in continued. 20% of ATR-IR spectra were selected as test and the rest of spectra were chosen as training data.

2.5. Model selection and validation

PLS-DA was performed on data as analytical model. Optimum amount of components were selected based on various amounts of three variables of data scaling, assignation criterion and cross validation (cv). Based on the minimum data error rate, final data was selected.

3. Results and discussion

3.1. Chemometrics model proportion

As mentioned before, IR data was converted to a matrix in which, response vector (Y values) are real amounts of sertraline and ATR-IR data at different wavenumbers were considered as X matrix. Baseline correction was achieved by means of SNV to disallow fluctuations of base line in different samples and X matrix data that developed different baseline were deleted. Final results after SNV operation is demonstrated in Figure 1.

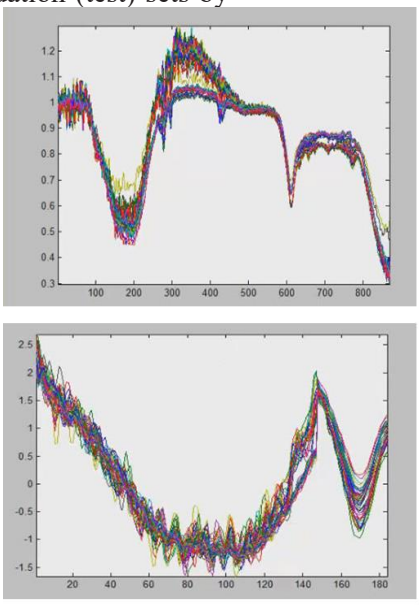

Figure 1. IR spectra as X matrix before (A) and after (B) SNV.

Table 2. Optimum amount of component with Number of cv groups=3.

Number of components	Data scaling	Assignation criterion	Cross validation	Error rate fitting	Error rate cv	Not assigned fitting	Not assigned cv
6	none	bayes	Venetian blinds	0	0. 04	0. 07	0. 49
5	Mean centering	bayes	Venetian blinds	0	0. 06	0. 07	0. 47
7	Auto scaling	bayes	Venetian blinds	0	0. 15	0. 05	0. 35
12	Auto scaling	bayes	Venetian blinds	0	0. 15	-------	0. 51
13	none	max	Venetian blinds	0	0. 24	-------	------
18	none	max	Venetian blinds	0	0. 24	-------	------
19	none	max	Venetian blinds	0	0. 24	-------	------
11	Mean centering	max	Venetian blinds	0	0. 14	-------	------
6	Auto scaling	max	Venetian blinds	0. 01	0. 19	-------	------
7	Auto scaling	max	Venetian blinds	0	0. 16	-------	------
10	Auto scaling	max	Venetian blinds	0	0. 17	-------	------

Table 3. Optimum amount of component with Number of cv groups=4.

Number of components	Data scaling	Assignation criterion	Cross validation	Error rate fitting	Error rate cv	Not assigned fitting	Not assigned cv
10	none	bayes	Venetian blinds	0	0. 14	-------	0. 33
11	none	bayes	Venetian blinds	0	0. 17	-------	0. 33
17	none	bayes	Venetian blinds	0	0. 16	-------	0. 47
9	Mean centering	bayes	Venetian blinds	0	0. 14	-------	0. 33
7	Auto scaling	bayes	Venetian blinds	0	0. 14	0. 05	0. 35
8	none	max	Venetian blinds	0	0. 17	-------	------
15	none	max	Venetian blinds	0	0. 18	-------	------
7	Mean centering	max	Venetian blinds	0	0. 15	-------	------
10	Auto scaling	max	Venetian blinds	0	0. 15	-------	------
7	Auto scaling	max	Venetian blinds	0	0. 16	-------	------
10	Auto scaling	max	Venetian blinds	0	0. 17	-------	------

Table 4. Number of components with minimum error rate fitting and error rate cv.

Number of components	11	7	7
Data scaling	Mean centering	Auto scaling	Mean centering
Assignation criterion	max	max	max
Cross validation	Venetian blinds	Venetian blinds	Venetian blinds
Number of cv groups	3	3	4
Error rate fitting	0	0	0
Error rate cv	0.14	0.16	0.15
Not assigned fitting	---	---	---
not assigned cv	---	---	---
Accuracy fitting	1	1	1
Accuracy cv	0.77	0.72	0.74
Error rate test	9%	0%	0%

3.2. Optimum amount of component

As they are shown in table 2 (Number of cv groups= 3) and table 3 (Number of cv groups= 4), based on different values for variable, following data are gathered:

Based on the obtained data, lower amounts of error rate cv and error rate fitting are selected as below:

As a result, when the number of components is 7, error rate test is zero. Results show that model was not produced randomly and the amount of sertraline can be determined correctly after omitting the effect of other excipients. As previously mentioned the main advantage of PLS-DA method is handling of highly noisy data and provides a visual interpretation of complex data (16, 17). Different variables are set in models and the main results are based on the error rates that show the predictability and the precision of the model. Zero error rates show that the model was able to separate and predict the training and test data and determine sertraline amounts with minimal error.

4. Discussion

An ATR-IR method was used to determine sertraline in a mixture of excipients. According to the results, this technique can be an alternative assay method in sertraline determination. The use of PLSDA model with 3 variables led to optimum prediction for sertraline concentration. In this study, different amounts of sertraline samples were prepared and their concentrations were evaluated by ATR-IR. The output data of ATR-IR was used as input data of chemometric model. The results ensure that sertraline amount obtained by simple method ATR-IR is similar to real amounts of the drug and this method can be used as a predictive and simple replacement in drug determination in different pharmaceutical studies. However, more operations with different drugs and excipients are needed.

Conflict of Interest

None declared.

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