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Simultaneous Estimation of Multicomponent Dosage Forms Using UV-Spectroscopy and Chemometric Approaches

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ABSTRACT

These days, UV-visible spectroscopy is widely used as a quick, easy, accurate, and very accurate technique for quantitative estimation. The fundamental idea behind this method is that the analyte concentration is directly correlated with the quantity of light absorbed. While multi-component analysis may be used on any degree of spectral overlap as long as two or more spectra are not precisely the same, the simultaneous equation is only useful for estimating medications whose spectra overlap appropriately. Before a medicine is introduced to the market, quantitative assessment is required since a formulation with a higher concentration may create toxicity issues, while one with a lower concentration may not work as intended.

Keywords: Area under Curve, Derivative, Isoabsorptive, Multicomponent Mode, Simultaneous Equation

INTRODUCTION

Because of its many uses, analytical chemistry is the scientific discipline that is beneficial in all areas of science and medicine. The two main facets of chemical characterisation that it addresses are qualitative (what it is) and quantitative (how much it is). One While quantitative analysis provides the numerical quantity of one or more components present, qualitative analysis exposes the sample's chemical identity.

The measurement of a characteristic that is proportionate to the quantity of analyte in the sample is the fundamental requirement underlying these techniques. These techniques fall into two categories: systemic or instrumental techniques like refractometry, colorimetry, absorptimetry, etc., and traditional techniques like gravimetry, volumetry, titrimetry, etc., depending on the property to be measured. 1, 2

The market is now overflowing with different dosage form combinations, and the number is growing daily. 3. These multi-component formulations are becoming more popular because of their improved potency, various actions, reduced side effects, faster relief, and higher patient acceptance. 4. As a result, it is intended that these formulations satisfy all quality, safety, and effectiveness criteria; this can only be achieved by analyzing them using various techniques. The goal of this quantitative assessment is to make sure that a given medicine has the same quantity of substance as stated because if the dose is too high, adverse effects from overdosing will occur, and if it is too low, the patient won't get the recommended dosage. Instrumental techniques such as spectrophotometry, HPLC, GLC, HPTLC, and others are used for the estimation of multi-component formulations because of their inherent benefits, which include avoiding time-consuming extraction and separation, being economical in that they require fewer costly regents, and being equally accurate and precise. The foundation of these techniques is the measuring of the drugs' unique and nonspecific physical characteristics.

In addition to the primary medications, the dose form may sometimes include other compounds that might interfere with the test and, if left unchecked, could cause a systemic mistake. One fundamental requirement is the development of novel techniques for simultaneous, interference-free drug analysis. For such medications, for which there is now no analytical method available for estimate, it becomes important to design new analytical techniques. To put it briefly, the following factors led to the creation of more recent drug analysis techniques: The medication or drug combination may not be recognized by any pharmacopoeia.

Because of patent constraints, there may not be analytical techniques for estimating the drug in combination with other pharmaceuticals or a valid analytical process for the drug in the literature. ¬ Expensive solvents and reagents may be needed for the current analytical processes. Additionally, it can include laborious extraction and separation processes, which might not be trustworthy. 1, 5 This review focuses on the UV-visible spectroscopic techniques for drug assessment.

Simultaneous Equation Method[6, 7, 8]

Consider a multicomponent system consisting of two components X and Y, each of which absorbs at the λmax of the other, λ_1 being the wavelength of maximum absorbance of X (λmax) and λ_2 being the wavelength of maximum absorbance of Y (λmax) (Fig.1.1.)

In such cases, it can be possible to determine both the components by simultaneous equation method. The information required is:

- The absorptivities of X at λ_1 and λ_2, ax_1 and ax_2 respectively.
- The absorptivities of Y at λ_1 and λ_2, ay_1 and ay_2 respectively.
- The absorbance of the diluted sample at $\lambda_1$and λ_2, A_1 and A_2 respectively.
- c_x and c_y be the concentrations of X and Y respectively in the diluted sample.

Thus the absorbance of the mixture at λ_1 and λ_2 may be expressed as follows:

$$A_1 = a_{X1}bc_X + a_{Y1}bc_Y \quad \text{.....At } \lambda 1 \text{ ..... (1)}$$

$$A_2 = a_{X2}bc_X + a_{Y2}bc_Y \quad \text{.....At } \lambda 2 \text{ ..... (2)}$$

For measurements in 1 cm cell, b = 1, therefore,

$$C_x = A_2a_{y1} - A_1a_{y2} / a_{x2}a_{y1} - a_{x1}a_{y2}$$

$$C_y = A_1a_{x2} - A_2a_{x1} / a_{x2}a_{y1} - a_{x1}a_{y2}$$

Using the above two equations the concentration of component X and component Y in the sample mixture can be determined.

The Absorption Ratio Method: Isoabsorptive Point Method[6]

This method is a modification of the simultaneous equations method. According to this method, the ratio of absorbance at any two wavelengths for a substance, which obeys Beer's law, is constant value independent of concentration and path length. This constant is termed as "Hufner's Quotient' or Q-value. This method involves the measurement of absorbance at two wavelengths, one being the λ max of one of the components (λ_2) and the other being a wavelength of equal absorptivity of the two components (λ_1), called as Iso-absorptive point (Fig. 1.2.).[5]

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The concentration of each component can be calculated by mathematical equation:

$$Cx = (Qm - Qy / Qx - Qy)^* A / a_1$$
$$Cy = (Qm - Qx / Qy - Qx)^* A / a_2$$

Where, Cx and Cy = concentration of x and y respectively,

A = Absorbance of sample at isoabsorptive wavelength,

a_1 and a_2 = Absorptivity of x and y respectively at isoabsorptive wavelength,

$Qm = \frac{\text{Absorbance of sample solution at } \lambda_{max} \text{ of one of the components } (\lambda_2)}{\text{Absorbance of sample solution at isoabsorptive wavelength}}$

$Qx = \frac{\text{Absorptivity of x at } \lambda_{max} \text{ of one of the components } (\lambda_2)}{\text{Absorptivity of x at isoabsorptive wavelength}}$

$Qy = \frac{\text{Absorptivity of y at } \lambda_{max} \text{ of one of the components } (\lambda_2)}{\text{Absorptivity of y at isoabsorptive wavelength}}$

Derivative Spectroscopic Method[6]

Derivative spectrophotometry involves the conversion of a normal spectrum (fundamental, zeroth order or D spectrum) to its first, second or higher derivative spectrum by differentiating absorbance of a sample with respect to wavelength λ for higher accuracy (Fig.1.3.).[4]

[A] = f (λ): zero order

[dA/dλ] = f (λ): first order

[$d^2A/d\lambda^2$] = f (λ): second order

The strong positive & negative bands with maximum and minimum at same wavelength of an absorption band as inflection point in absorbance band governs the odd (first & third) derivative spectrum whereas the strong positive & negative band with minimum or maximum at same wavelength as λmax of absorbance band governs the even (second & fourth) derivative spectrum.[10]

Number of bands = Derivative order + 1

The amplitude (D) is directly proportional to the concentration of analyte provided Beer's law is obeyed by D° spectrum.

In first order derivative spectroscopy, zero crossing point for both drugs is found and the wavelengths are selected in a manner such that at the zero crossing of one drug, the other drug should show substantial absorbance.

Advantages:

- It enhances resolution permitting identification of analyte with close λmax.
- It eliminates baseline shift effect arising from instrument or sample handling.
- It eliminates scattering effects thus helpful for analyte present in turbid solution.[11]

Multicomponent Mode Method

This method requires two wavelengths. One wavelength is selected such that one drug shows maximum absorbance while other drug shows considerable absorbance. The second wavelength is selected such that other drug shows maximum absorbance while the first one shows considerable absorbance.

Consider a mixture consisting of two components M and N where X_1 nm and X_2 nm are the maximum absorbance of component M and N respectively (Fig.1.4.)

The absorbance of mixture containing components M and N at wavelength X_1 and X_2 may be expressed as follows,

$$A' = E'_M BC_M + E'_N BC_N \text{ ---------- at } X_1$$
$$A'' = E''_M BC_M + E''_N BC_N \text{ ---------- at } X_2$$

Using individual standard solution of M and N, the two absorptivities (E'_M, E'_N) at one wavelength and the other two absorptivities (E''_M, E''_N) at the other wavelength can be determined. The absorbance of the mixture A' and A'' are experimentally determinable and thus from the above two equations the concentration of the individual constituents C_M and C_N can be readily calculated. This relationship is valid if Beer's law is followed and both the components behave independently of one another. Choosing wavelengths at which the differences in molar absorptivities are large, leads to attain greater accuracy in this analysis.

Area Under Curve Method[6-9]

This method also utilizes two wavelength ranges. From the overlain spectra of both drugs the area under curve is determined at both the selected analytical wavelength ranges. Within the above selected wavelength ranges, the area under curve was determined for both the drugs and analysis was performed using "Cramer's Rule" and "Matrix Method".

Consider a binary mixture consisting of two components M and N. From the two spectra (Fig.1.5. and Fig.1.6.) following information are obtained:

- $AUC^M_{\lambda_1 - \lambda}$: area under curve for component M at the wavelength range $\lambda_1 - \lambda_2$.
- $AUC^M_{\lambda_3 - \lambda}$: area under curve for component M at the wavelength range $\lambda_3 - \lambda_4$.
- $AUC^N_{\lambda_1 - \lambda}$: area under curve for component N at the wavelength range $\lambda_1 - \lambda_2$.
- $AUC^N_{\lambda_3 - \lambda}$: area under curve for component N at the wavelength range $\lambda_3 - \lambda_4$.

The total area under the curve of a mixture at a particular wavelength range is equal to the sum of area under curve of the individual components at same wavelength range. The area under curve of the mixture containing component M and N can be given as follows:

$$AUC_{\lambda_1 - \lambda_2} = AUC^M_{\lambda_1 - \lambda_2} + AUC^N_{\lambda_1 - \lambda_2} \text{ ----------} (1)$$
$$AUC_{\lambda_3 - \lambda_4} = AUC^M_{\lambda_3 - \lambda_4} + AUC^N_{\lambda_3 - \lambda_4} \text{ ----------} (2)$$

Now the above equation can also be written as follows:

$$AUC_{\lambda_1 - \lambda_2} = X^M_{\lambda_1 - \lambda_2} bC^M + X^N_{\lambda_1 - \lambda_2} bC^N \text{ ----------} (3)$$

$$AUC_{\lambda_3 - \lambda_4} = X^M_{\lambda_3 - \lambda_4} bC^M + X^N_{\lambda_3 - \lambda_4} bC^N \text{ ----------} (4)$$

Where, $X_{\lambda_1 - \lambda_2} = AUC_{\lambda_1 - \lambda_2} /$ Conc. in g/l

$X_{\lambda_3 - \lambda_4} = AUC_{\lambda_3 - \lambda_4} /$ Conc. in g/l

By applying "Cramers Rule" and "Matrix Method", the concentration of component M and component N can be determined as follows:

$$C^M = \frac{X^N_{\lambda_1 - \lambda_2} AUC_{\lambda_3 - \lambda_4} - X^N_{\lambda_3 - \lambda_4} AUC_{\lambda_1 - \lambda_2}}{X^M_{\lambda_1 - \lambda_2} X^N_{\lambda_3 - \lambda_4} - X^N_{\lambda_3 - \lambda_4} X^M_{\lambda_1 - \lambda_2}} \text{ ----------} (5)$$

$$C_N = \frac{X^M_{\lambda_1 - \lambda_2} AUC_{\lambda_3 - \lambda_4} - X^M_{\lambda_3 - \lambda_4} AUC_{\lambda_1 - \lambda_2}}{X^M_{\lambda_1 - \lambda_2} X^N_{\lambda_3 - \lambda_4} - X^N_{\lambda_3 - \lambda_4} X^M_{\lambda_1 - \lambda_2}} \text{ ----------} (6)$$

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From the study, it has been found that so many combinations have been successfully estimated by UV-Visible spectroscopic methods like combinations of Diclofenac sodium and tizanidine[10], Pantoprazole & domperidone[11], Dexibuprofen & Paracetamol[12], Enalapril maleate & Amlodipine besylate[13], Sulphamethaxole & Trimethoprin[14], Rabeprazole and Itopride[15], Ondansetron and Paracetamol[16], Ofloxacin and Satranidazole[17], Nebivolol and Hydrochlorothiazide[18], Metronidazole & Amoxicillin[19], Norfloxacin & Ornidazole[20], Ofloxacin & Ornidazole[21]etc.

CONCLUSION

We may conclude that UV-visible spectroscopy is a straightforward, time-efficient, accurate, and highly sensitive approach that can be used to estimate various drug combinations for which no estimation method has been published to date.

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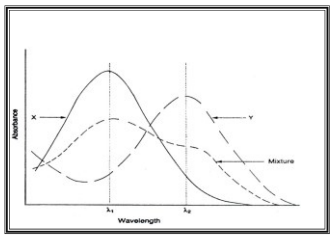

Fig: 1.1. Overlain spectra of component X, Y and Mixture containing X & Y

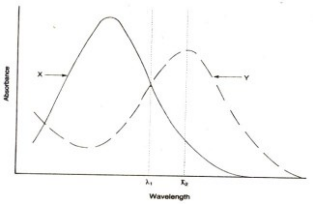

Fig: 1.2. Overlain spectra of component X and Y.

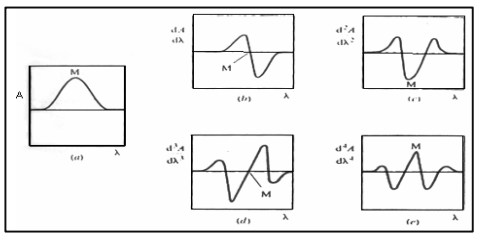

Fig.1.3 Zero, First, Second, Third and Fourth order derivative spectra of gaussian peak

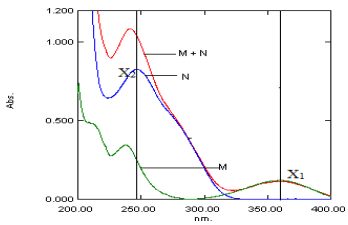

Fig: 1.4. Overlain spectra of component M, N and Mixture containing M & N.

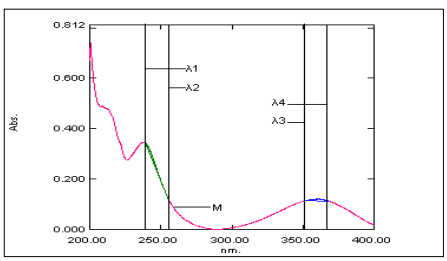

Fig: 1.5. Spectra showing Area under Curve for drug M.

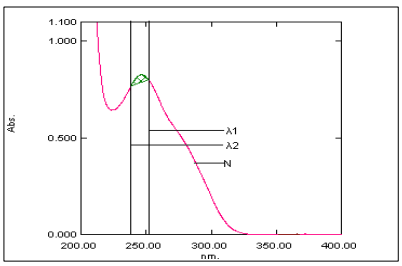

Fig: 1.6. Spectra showing Area under Curve for drug N