INTERNATIONAL RESEARCH JOURNAL OF PHARMACY ISSN 2230 – 8407
Available online www.irjponline.com Review Article

SIMULTANEOUS ESTIMATION OF MULTICOMPONENT FORMULATIONS BY UV-VISIBLE SPECTROSCOPY: AN OVERVIEW

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Article Received on: 14/10/11 Revised on: 20/11/11 Approved for publication: 29/12/11

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ABSTRACT
UV-visible spectroscopy, a simple, rapid, precise and highly accurate method for quantitative estimation is in great use now a day. The basic principle behind this technique is that the amount of light absorbed is proportional to the concentration of analyte. Simultaneous equation is applicable for the estimation of those drugs where the spectra of drugs overlap properly whereas multi-component analysis can be applied on any degree of spectral overlap provided that two or more spectra are not similar exactly. Quantitative estimation is necessary before introduction of any drug into the market as either concentration is more in formulation can cause toxicity problem or if concentration is found less, then formulation may not be effective in prescribed dose.
Keywords: Simultaneous equation, Isoabsorptive, Derivative, Multicomponent Mode, Area under Curve

INTRODUCTION

Analytical chemistry is the branch of science which is useful in all fields of science and medicine due to its versatile applications. It deals basically with the two aspects of chemical characterization i.e. qualitative (what it is) and quantitative (how much it is).[1] The qualitative analysis reveals the chemical identity of the sample while quantitative analysis gives the amount of one or more components present in numerical terms.

The basic criterion behind these methods is the measurement of some property which is proportional to amount of analyte in sample. Depending on the property to be measured, these methods are classified as classical methods such as gravimetry, volumetry, titrimetry, etc and systemic or instrumental methods like refractometry, colorimetry, absorptimetry etc.[1, 2]

In present era, market is flooded with various combinations in dosage forms and the number is increasing day by day.[3] These multi-components formulations due to greater patient acceptability, increased potency, multiple action, fewer side effects and quicker relief are gaining interest.[4] Therefore, it is desired that these formulations meet all the standards related to their quality, safety & efficacy and this can only be possible if they are analyzed by different methods. The motto behind this quantitative estimation is to ensure that whether a particular drug contains the same amount of drug as mentioned because if the dose given will be high then it will cause over dosage side effects & if it is less then the patient will not get the required dose. For the estimation of multi-component formulation, the instrumental techniques like Spectrophotometric, HPLC, GLC, HPTLC etc are employed due to their inherent advantages viz. avoid time consuming extraction and separation, economical in the sense that use of expensive regents is minimized, equally accurate and precise. These methods are based upon the measurement of specific and nonspecific physical properties of the substances.

Sometimes the dosage form in addition to the main drugs known to contain other substances which potentially interfere in the assay and if not corrected may impart a systemic error to the assay. The need to develop new methods to analyze the drugs simultaneously and without interferences is a basic need. Thus, it becomes necessary to develop new analytical methods for such drugs for which no analytical method is still available for estimation. In brief the reasons for the development of newer methods of drugs analysis are:

- The drug or drug combination may not be official in any pharmacopoeias.
- A proper analytical procedure for the drug may not be available in the literature due to patent regulations.
- Analytical methods for the estimation of drug in combination with other drugs may not be available.
- The existing analytical procedures may require expensive reagents and solvents. It may also involve cumbersome extraction and separation procedure and these may not be reliable.[1, 5]

The UV-Visible spectroscopic methods for estimation of drugs are highlighted in this review.

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]

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,

$A' = E'_M BC_M + E'_N BC_N$ ----------at X_1

$A'' = E''_M BC_M + E''_N BC_N$ ----------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:

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

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

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

Now the above equation can also be written as follows:

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

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

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:

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

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

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

It can be concluded that UV-visible spectroscopy can be effectively used for estimation of many drug combinations for which no method of estimation has been reported so far and it is simple, less time consuming, accurate and highly sensitive.

ACKNOWLEDGMENT

The authors are very thankful to the management of Maharishi Markandeshwer University, Mullana (Ambala) for constant support.

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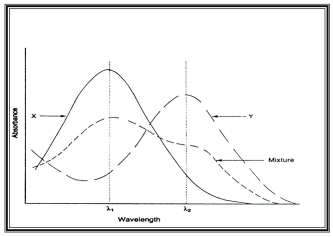

Fig: 1.1. Overlain spectra of component X, Y and Mixture containing X & Y

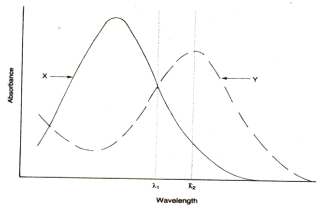

Fig: 1.2. Overlain spectra of component X and Y.

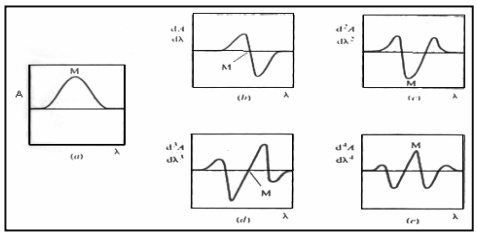

Fig.1.3 Zero, First, Second, Third and Fourth order derivative spectra of gaussian peak

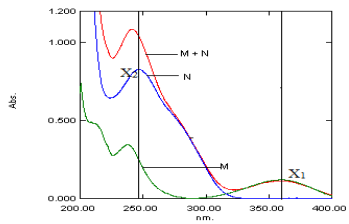

Fig: 1.4. Overlain spectra of component M, N and Mixture containing M & N.

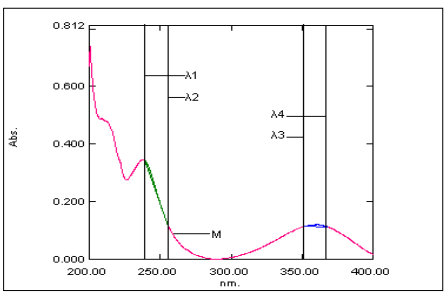

Fig: 1.5. Spectra showing Area under Curve for drug M.

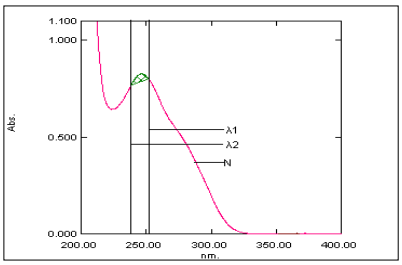

Fig: 1.6. Spectra showing Area under Curve for drug N