PHARMACEUTICAL ANALYSIS BY SIMULTANEOUS EQUATION METHODS: REVIEW

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ABSTRACT:

This approach can be used to estimate medications whose spectra appropriately overlap, i.e. It is possible to identify both medicines using the simultaneous equation method if a sample includes two absorbing medications, each of which absorbs at the λmax of the other.
The list of numerous mixed dose forms and food samples that were examined using Vierodt's approach is
contained in this article. This method makes it possible to determine a mixed dose form simply, quickly, and directly without any prior separation; as a result, it can be utilized in routine analysis. Since simultaneous estimating is both practical and time-saving, it is crucial in the pharmaceutical industry. The identification of the chemical entities in the pharmaceutical formulation is specific and assured by the simultaneous analytical examination. The analytical estimation's primary goal is to guarantee that the specific formulation has the same quantity of active medicinal ingredient as stated on the label.

Keywords: Simultaneous Equation, Spectroscopic Method, Method Development and Validation.

INTRODUCTION:

A multicomponent analysis is the simultaneous equation approach. Additionally called Vierordt's Method. In the domains of clinical chemistry, pharmaceutical drug analysis, pollution management, and other analytical chemistry fields, multicomponent analysis has recently emerged as one of the most fascinating issues. Multicomponent analysis can be used with a variety of analytical methods. Spectrophotometry, Chromatography, and Electrophoresis are a few examples [1].

Simultaneous Equation Analysis (Vierordt's Method)

It may be possible to identify the two species using Vierordt's approach if a sample contains two absorbing species (X and Y) that each absorb at the λmax of the other. The technique is predicated on the observation that the mixture's absorbance at any λ is equal to the sum of the absorbances of the X and Y species assuming that there is no physical or chemical interaction between the two elements [2].

It has been seen that UV/ VIS absorption peaks are generally broad, so if there are two compounds, X and Y in solution, it is likely that they will not be completely resolved from each other. That is, both X and Y contributes to the absorbance at most wavelengths. It is possible to calculate the concentration of X and Y from a series of measurements [2].

Measurements must be made at a number of wavelengths equal to the number of components in the mixture. If there are two components, two wavelengths are needed. Four calibration curves need to be prepared: X at λ1, X at λ2, Y at λ1, and Y at λ2. All calibration curves should be blank corrected to pass through the origin. The absorbance of sample mixture is measured at λ1 and λ2.

Procedure:

Each component's λmax value is calculated using a solution at the appropriate concentration. Plotting absorbance values vs. concentration allows the Beer's law to be checked at each respective λmax for the solutions of adequate concentrations of each component. This is the component's calibration curve at its λmax value. Determined is cuvette is used to calculate the absorbance values of the combination at each wavelength. The measurements collected in this manner are included in the subsequent equations:

Simultaneous Equation Analysis

Two equations can be written:

1. $A^{\lambda 1} = \left(A_\chi^{\lambda 1} + A_y^{\lambda 1}\right) = \left(\varepsilon_\chi^{\lambda 1} C_\chi\right) + \left(\varepsilon_y^{\lambda 1} C_y\right)$

2. $A^{\lambda 2} = \left(A_\chi^{\lambda 2} + A_y^{\lambda 2}\right) = \left(\varepsilon_\chi^{\lambda 2} C_\chi\right) + \left(\varepsilon_y^{\lambda 2} C_y\right)$

Where,

$A^{\lambda 1}, A^{\lambda 2}$ are the absorbances of unknown at λ_1 and λ_2.

C_χ, the concentration of X in the unknown; C_y, the concentration of Y in the unknown.

$\varepsilon_\chi^{\lambda 1}$, the slope of the calibration curve for X at λ_1; $\varepsilon_\chi^{\lambda 2}$, the slope of the calibration curve for X at λ_2.

$\varepsilon_y^{\lambda 1}$, the slope of the calibration curve for Y at λ_1; $\varepsilon_y^{\lambda 2}$, the slope of calibration curve for Y at λ_2.

λ_1, λ_2 are the max of X and Y respectively [2].

APPLICATIONS OF SIMULTANEOUS EQUATION METHOD

I. New simple spectrophotometric method for the simultaneous estimation of paracetamol and flupirtine maleate in pure and pharmaceutical dosage form[3] :

For the simultaneous estimation of paracetamol and flupirtine maleate in pure and pharmaceutical dosage form, the Vierordt's approach, also known as the simultaneous equation method, was created and verified. The technique was based on the measurement of absorbance at two wavelengths, 245 nm and 344.5 nm, which corresponded to the maximum concentrations of flupiritine maleate and paracetamol in 0.1 N HCl. In the concentration ranges of 5–15 μg/mL and 1.53–4.61 μg/mL, respectively, the calibration curves for paracetamol and flupiritine maleate were found to be linear, with correlation coefficient values (R2) of 0.999. For paracetamol, the LOD and LOQ were 185.90 ng/mL and 563.38 ng/mL, and for flupiritine maleate, they were 78.89 ng/mL and 239.06 ng/mL. The percentage RSD value in the precision study was found to be within bounds (RSD 2%). The percentage recovery ranged from 99.18 to 100.02% for paracetamol and from 98.47 to 100.09% for flupiritine maleate at different concentration levels, demonstrating the accuracy of the projected approach. The results of the inquiry might be used to draw the conclusion that the method for simultaneous estimate of paracetamol and flupirtine maleate in pure and tablet dose form is straightforward, accurate, exact, and cost-effective. For the simultaneous measurement of paracetamol and flupiritine maleate in pure and pharmaceutical dosage form, the suggested approach can be used successfully.

II. Applications of simultaneous equation method and derivative method for the determination of rabeprazole sodium and levosulpiride in pharmaceutical dosage form and dissolution samples[5] :

For the simultaneous estimate of rabeprazole sodium and levosulpiride in combination tablet dose form, two straightforward, accurate, exact, and affordable techniques have been established. These processes don't require laborious sample preparation or extraction operations. The initial approach was based on analysing both medications simultaneously using equations. Levosulpiride and rabeprazole sodium both have absorbance maxima in methanol at 284 and 232 nm, respectively. The second method was based on a derivative spectrophotometric method that involved locating each drug's zero crossing point (ZCP) in turn. The determinations for the rabeprazole sodium and levosulpiride first order derivative spectra were made at 231.2 nm (ZCP of levosulpiride) and 246.2 nm (ZCP of rabeprazole sodium), respectively. For both medicines, the linearity was observed in the concentration range of 1–20 lg/ml. 900 cc of phosphate buffer with a pH of 7.4 was employed as the dissolving media in a USP type 2 apparatus with a stirring speed of 100 rpm. The drug release was assessed using spectroscopic techniques that were developed. The developed method's suitability for quantifying rabeprazole sodium and levosulpiride was demonstrated through validation.

III. Two different spectrofluorimetric methods for simultaneous determination of gemfibrozil and rosiglitazone in human plasma[6] :

Without the need for previous separation procedures, two precise, dependable, and highly sensitive spectrofluorimetric techniques were created for the simultaneous determination of the binary combination of gemfibrozil and rosiglitazone in human plasma. The first technique makes use of multiple scans in synchronous fluorescence spectrometry. Gemfibrozil produces a discernible signal at $\Delta\lambda = 27$ nm regardless of the presence of rosiglitazone. Similar to this, the presence of gemfibrozil at $\Delta\lambda = 120$ nm had no effect on the signal of rosiglitazone. Gemfibrozil and rosiglitazone concentrations fluctuate linearly with signals at two wavelengths, 301 ($\Delta\lambda= 27$ nm) and 368 ($\Delta\lambda= 120$ nm), over the ranges of 100-700 ng mL^{-1} (for gemfibrozil) and 20-140 ng mL^{-1} (for rosiglitazone), respectively. For gemfibrozil and rosiglitazone, the limits of detection (LOD) were 2.3 and 2.72 ng mL^{-1}, respectively. The second method uses 258 nm as the excitation wavelength and is based on the simultaneous equations method (Vierordt's method). On the basis of the fact that the fluorescence of the mixture is equal to the sum of the individual fluorescences of gemfibrozil and rosiglitazone at (λ_{Em2}=302nm for gemfibrozil) and (λ_{Em2}=369nm for rosiglitazone). For gemfibrozil and rosiglitazone, the limits of detection (LOD) were 28.1 and 23.63 ng mL^{-1}, respectively. The two chemicals were identified using the suggested procedures with excellent recovery in both synthetic mixtures and human plasma.

IV. Application of different spectrophotometric methods for simultaneous determination of elbasvir and grazoprevir in pharmaceutical preparation [7] :

Elbasvir and grazoprevir are two newly FDA-approved medications that have been simultaneously determined using the first three UV spectrophotometric methods using their combined pharmaceutical dose form. These techniques include simultaneous equations

and partial least squares, both with and without a genetic process for variable selection. The absorbance values at 369 nm (the λmax value for elbasvir) and 253 nm (the λmax value for grazoprevir) have been chosen for the simultaneous equation approach in order to create the two simultaneous equations necessary for the mathematical processing and quantitative analysis of the medications under study. Instead of using a single or dual wavelength, the partial least squares with and without variable selection procedure (genetic algorithm) has been applied in the analysis of spectra because it greatly improves the precision and predictive power of the methods by synchronously including many unreal wavelengths. The suggested procedures have been used to test the medicines in their pharmaceutical formulation successfully. A statistically based comparison of the results with the manufacturing processes has been done. It is important to highlight that there were no appreciable differences in the validation parameters between the suggested methods and the production one.

V. Validation and application of vierordt's spectrophotometric method for simultaneous estimation of tamoxifen/coenzyme q10 in their binary mixture and pharmaceutical dosage forms[9]:

Both TC and CoQ10 were created as solid lipid nanoparticles (SLNs) in order to increase patient compliance and the sustainability of the chemotherapeutic healthcare system. The goal of the study was to develop and validate a straightforward and repeatable spectrophotometric method for measuring TC and CoQ10 simultaneously in binary mixtures or pharmacological dose forms. The development of a new technique based on simultaneous estimation of drug mixtures without prior separation. The International Conference on Harmonisation (ICH) guidelines were compared to the validation parameters. Statistics were used to compare the suggested approach to HPLC in terms of accuracy and reproducibility. At absorptivity wavelengths of 236 nm and 275 nm, respectively, the amounts of TC and CoQ10 were measured. Beer's law was followed by calibration curves in the 2–14 μg/ml range for both methanol and simplified simulated intestinal fluid (SSIF), with an R2 correlation coefficient of 0.999. The percentage implies recovery of TC and CoQ10 in their pure form or in a binary mixture at varied concentration levels were all close to 100%. The proposed method's great precision and accuracy are confirmed by the low values of SD and %RSD (2%). Different % means recovery were seen in the developed SLNs, ranging from 32-59% for CoQ10 and 81-92% for TC. In comparison to HPLC, the results produced by simultaneously using Vierordt's equations exhibited little statistical significance. The Vierordt method was successfully used to estimate the amounts of TC and CoQ10 in pure state, binary mixtures, and pharmaceutical dose forms. It is straightforward, accurate, precise, and affordable.

VI. Simultaneous estimation of dutasteride and tamsulosin hydrochloride in tablet dosage form by vierordt's method[8]:

Dutasteride (DU) and tamsulosin hydrochloride (TA) are simultaneously estimated in pure and pharmaceutical dosage form using the new vierordt's (VI) approach, also known as the simultaneous equation (SE) method, which is straightforward, quick, and accurate. The procedure relies on the measurement of absorbance at two wavelengths, 240.6 nm and 279.4 nm, which correspond to the λmax of DU and TA in methanol, respectively. In the concentration ranges of 20–40 μg/ml for DU and 16–32 μg/ml for TA, calibration curves are linear. Studies on LOD, LOQ, precision, and recovery are computed. For the simultaneous determination of DU and TA in pure and medicinal dosage form, the suggested method is successfully used.

VII. Simultaneous determination of indigotin and ponceau-4r in food samples by using vierordt's method, ratio spectra first order derivative and derivative uv spectrophotometry [10]:

First order derivative UV spectrophotometry, ratio spectra first order derivative, and Vierordt's method are three sensitive and precise techniques for determining Indigotin and Ponceau-4R in mixes. For these new techniques, there was no separating phase necessary. In the wavelength range of 300-700 nm and phosphate buffer pH 7.0 medium, ratio spectra first order derivative and first derivative UV spectrophotometric approaches were investigated. At established UV spectrophotometric methods, the linearity ranges were discovered to be 1.00-50.00 μg ml1 for Indigotin and 1.00-52.00 μg ml1 for Ponceau-4R dyes. The commercially available food samples containing saccharose and citric acid, such as powdered drinks, sweets, and jellies, were subjected to these processes in order to identify both colors. For the analysis of Indigotin and Ponceau-4R in food samples, developed spectrophotometric methods were found to be accurate, precise, repeatable, directly applicable, and simple to use.

Data from previously reported HPLC methods were compared with data from these spectrophotometric methods to identify Indigotin and Ponceau-4R dyes in food. There was no statistically significant difference between these two approaches.

VIII. A comparative study of the ratio spectra derivative spectrophotometry, Vierordt's method and high- performance liquid chromatography applied to the simultaneous analysis of caffeine and Paracetamol in tablets[11]:

High-performance liquid chromatography and two spectrophotometric techniques were suggested for the simultaneous measurement of caffeine and paracetamol in a tablet formulation. The first derivative of the ratio spectra's analytical signals, measured at 267.9 and 291.0 nm for caffeine and 237.0 and 251.8 nm for paracetamol are used as the basis for the ratio spectra derivative method. For caffeine and paracetamol, calibration graphs were created in the 4–40 μg/ml and 8–48 μg/ml ranges, respectively. Caffeine and paracetamol A11 (1%, 1 cm) values were found in zero-order spectra at 242.9 and 273.0 nm using Vierordt's technique. With the help of the software program "Matlab" the matrix for A11 (1%, 1 cm) values was written and the amounts of both medications were determined. The outcomes obtained by these spectrophotometric methods were compared with the results of HPLC method.

IX. Simultaneous spectrophotometric method for determination of emtricitabine and tenofovirdisoproxil fumarate in three-component tablet formulation containing rilpivirine hydrochloride[12]:

It is extremely difficult to develop a single analytical technique for estimating a single drug from a multi-drug combination. For the simultaneous estimation of some antiviral medications, including emtricitabine (EMT), tenofovir disoproxil fumarate (TDF), and rilpivirine

HCl (RPV) in tablet dosage form, a complexation, derivatization, extraction, and sensitive-free direct UV spectrophotometric method is developed and validated. The standard and sample solutions were made in methanol. Emtricitabine, tenofovir disoproxil

fumarate, and rilpivirine hydrochloride all had different λmax values of 240.8 nm, 257.6 nm, and 305.6 nm. In the concentration ranges of 4–12 μg/ml for EMT, 6–18 μg/ml for TDF, and 0.5–1.5 μg/ml for RPV, respectively, calibration curves are linear. The study and validation of the simultaneous equation method's results for various parameters according to ICH guidelines.

X. Simultaneous spectrophotometric methods for estimation of levocetirizine and pseudoephedrine in pharmaceutical tablet dosage form[4] :

Levocetirizine dihydrochloride (LEVC) and pseudoephedrine hydrochloride (PSEUDO) simultaneous estimating techniques have been developed for two component solid dosage forms. The techniques use the absorbance ratio (Q-analysis) approach and simultaneous equations. These procedures all use distilled water as the solvent. PSEUDO exhibits maximum absorbance at 257 nm, while LEVC exhibits maximum absorbance at a wavelength of 231 nm. The linearity ranges for LEVC and PSEUDO were 5-30 μg/ml and 120-960 μg/ml, respectively. The linearity ranges for LEVC and PSEUDO were 5- 30 μg/ml and 120- 960 μg/ml, respectively, when the ratio of absorbance at 231 nm (the highest absorption of LEVC) and isobestic wavelength 242 nm was determined. The methods were effectively used for the concurrent determination of both medicines in lab-prepared mixes and in the manufacturing of commercial tablets. Recovery studies evaluated the approaches' accuracy, which ranged from 97.87 to 99.70% for LEVC and 99.01 to 99.79% for PSEUDO using the simultaneous equation method and from 98.99 to 101.42% for LEVC and 99.57 to 99.91% for PSEUDO using the graphical absorbance ratio method.

CONCLUSION:

The results of the research have led to the conclusion that the assessment of medication combinations can benefit from the use of analytical approaches. For research purposes where no new approach of estimating and analysis has been disclosed yet, the compensation for doing simultaneous estimation is rapid, straightforward, less time-consuming, precise, and sensitive. Thus, for the needs of the pharmaceutical industry, simultaneous examination utilizing a range of analytical techniques is extremely expensive.

ACKNOWLEDGEMENTS:

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