FIRST ORDER, SECOND ORDER, AND THIRD ORDER DERIVATIVE UV-SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION: A REVIEW

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ABSTRACT

Background: Derivative spectroscopy came into existence in the 1950s as it was advantageous in several aspects which includes effortless multicomponent analysis, elimination of unnecessary background absorption, resolution of overlapping bands, and qualitative and quantitative analysis. Higher order derivative spectra are obtained here such as, first order spectra, second order spectra, third order spectra etc.

Main body: In this review paper, we have concentrated mainly on first, second, and third order derivative spectrophotometric method development and validation of several medications that are either present singly or in combination in the formulation.

Short conclusion: From the review we can conclude that derivative spectrophotometric methods have accelerated and eased the process for analysing the given sample using a broad range of solvents.

Keywords Derivative Spectroscopy, First order derivative spectrum, Second order derivative spectrum, Third order derivative spectrum.

Background

UV-Vis Spectroscopy is a quantitative approach where one can measure how much light a chemical substance preoccupies. The UV radiation has adequate energy to excite valance electrons in various atoms or molecules, as a result UV is associated with electronic excitation. Spectroscopically , visible light performs in the same way as UV light ; therefore it is normally considered part of the electronic excitation region .Here we compute the intensity of light that passes through a sample with respect to the intensity of the light that cross through a reference sample or blank.[1]

UV spectrometer also known as absorption spectrophotometer and molecular electronic absorption spectrometer is a section of equipment that includes light source; a holder for the sample; a diffraction grating or monochromator to segregate the different wavelengths of light and to estimate the spectra in the range ultraviolet to visible (190—800 nm) , a detector is used.UV spectrometer is applied in analytical chemistry for the quantitative establishment of analytes, like transition metal ions, thoroughly combined organic compounds, and biological macromolecules.[2]

To filter undesired contents in the source spectrum, an operative approach is discussed which is known as derivative spectroscopy. The transfer function available for the method is obtained in the conceptual analysis, and the advantages convenient by this method are conversed in relation with this transfer function. Derivative spectroscopy is used in the elucidation and exploitation of data received from rapid-scan UV—VIS absorbance detectors for discovering the clarity of chromatographic peaks.UV spectrometer is applied in analytical chemistry for the quantitative establishment of analytes, like transition metal ions, thoroughly combined organic compounds, and biological macromolecules.It is a spectroscopic method that transforms spectra's mostly in the IR, UV-Visible absorption and Fluorescence spectrometry. Derivative methods are used in the analytical chemistry for the Spectral differentiation, Spectral resolution enhancement and Quantitative analysis. [3-5].(Fig. 1)

TYPES OF UV SPECTROSCOPY:

1. Zero order derivative spectrum.
2. First order derivative spectrum.
3. Second order derivative spectrum.
4. Third order derivative spectrum.
5. Fourth order derivative spectrum.

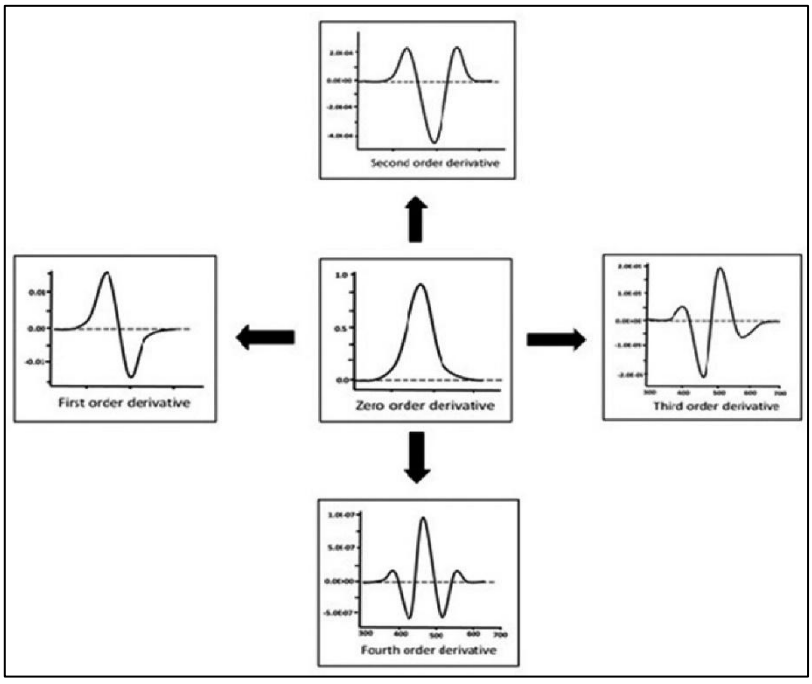

Fig. 1. Order of Derivative Spectra

FIRST ORDER DERIVATIVE

A first-order derivative is the rate of change of absorbance regarding wavelength. At zero, the first order derivative starts and finishes. It also proceeds towards zero at a similar wavelength as lambda max of the absorbance band. One of the two sides are positive or negative bands with maximum and minimum at the identical wavelengths as the inflection points in the

absorbance band.One of the two sides of this points are positive and negative bands with maximum and Minimum at the similar wavelengths as the inflection points in the absorbance band.[5]

$$dA/d\lambda = f'(\lambda)$$

SECOND ORDER DERIVATIVE

Second order derivative involves converting of the instrumental spectrum by premeditating and plotting the spectrum curve into a second derivative, which can amplify resolution bands, decrease background and matrix interference, and furnish qualitative and quantitative information and it is a plot of curvature of absorption spectrum against wavelength.The second order derivative is used as a tool for quantitative analysis, manifestation and quality control in agricultural, industrial, pharmaceutical and biogeochemical fields.[6]

$$d^2A/d\lambda^2 = f'(\lambda)$$

THIRD ORDER DERIVATIVE

Unlike second order spectrum third derivative spectrum shows disperse function to that of original curve.[6]

$$d^3A/d\lambda^3 = f''(\lambda)$$

Main text

1. NaziraSarkis*et al*., [7], have reported the development and validation of an accurate and precise derivative UV spectroscopic method for simultaneous estimation of nicotinamide (NCT) and tretinoin (TRT) in a binary mixture of dermal pharmaceutical preparations i.e., solution and cream with a ratio of 1:40 (TRT: NCT). They have used methanol as a solvent to dissolve pure NCT, pure TRT and binary mixture of both. Due totwo complications, first and second derivatives (D_1 and D_2) were produced. In case of first-order derivative, zero-crossing point for TRT (at concentration in the middle of 1.0-3.0 µg/ml) and its pharmaceutical preparations spectra was found at 253 nm whereas, NCT (at concentration 30 µg/ml) had a distinct peak at this wavelength. The zero-crossing points for TRT and its preparations spectra for second-order derivative was found at 245 nm and 269 nm whereas, NCT showed a sharp peak. For cream formula, 269 nm was the only choice in second-order derivative. This method was validated and three wavelengths 253 nm (D_1), 245nm (D_2) and 269 nm (D_2) were used to study the linearity of NCT while, the linearity for TRT was studied at 348 nm (D_0). The linearity range for NCT at all three wavelengths (D_1, D_2, D_2) and TRT was observed to be 10-80 µg/ml, 20-120 µg/ml, 10-120 µg/ml, and 0.5-5.0 µg/ml along with correlation coefficient (r^2) of 0.9996, 0.9998, 0.9999, and 0.9999, LOD (limit of detection) of 4.50 µg/ml, 5.60 µg/ml, 1.50 µg/ml, and 0.007 µg/ml, and LOQ (limit of quantitation) of 13.60 µg/ml, 16.80 µg/ml, 4.30 µg/ml, and 0.021 µg/ml, respectively. As per stability studies, TRT is stable in methanol for not more than 3 days when kept at room temperature.

2. J. S. Millership*et al*., [8], have reported thedetermination of simvastatin in tablet formulations by derivative UV spectroscopic methods i.e., zero, first and second order derivative methods. They have prepared a stock solution of simvastatin using methanol as

the solvent and diluted it to prepare solutions in the concentration range of 2 to 14 mg/L which showed absorption maximum (lambda max) at238 nm. At this wavelength the calibration curves for 1^{st} and 2^{nd} order derivatives were found to be linear in the above mentioned concentration range. This experiment was conducted in order to check the effect of excipients present in the tablet formulation on the absorbance of simvastatin. It was seen that due to the presence of ascorbic acid, an excipient used in the formulation, imprecise results were obtained but this problem was subdued by using 1^{st} and 2^{nd} order derivative spectra. Another problem that was encountered during the study was the degradation complex of simvastatin, simvastatin β-hydroxy acid which showed spectrum similar to that of parent compound. However, these two issues can be solved by using HPLC methods.

3. D. Madhuri*et al*., [9], have reported direct and derivative spectrophotometric estimation of Gemifloxacin mesylate (GFX) by chelation with palladium (II) ion. In aqueous environment, they synthesized chelate between GFX and palladium (Pd II). 1^{st} order derivative was seen at 480 nm and 2^{nd} order derivative at 500 nm. The chelate formed was linear over the concentration range of 1 to 10 µg/ml for 1^{st} order derivative whereas 1 to 15 µg/ml for 2^{nd} order derivative and has apparent molar absorption activities of 9.37x 10^4 L-$M^{-1}Cm^{-1}$ and 1.59x10 L-$M^{-1}Cm^{-1}$, respectively, for 1^{st} order derivative and 2^{nd} order derivative. While the limit of quantification ranged between 1.79 and 2.39, the limit of detection does not surpass 0.6. The correlation coefficient (r^2) was in the range of 0.998-0.999. Percentage recoveries were 100.02±0.177 for 1^{st} order and 100.045±0.139 for 2^{nd} order, according to the findings obtained by using this methodology.

4. Mahesh Attimarad*et al*., [10], have reported simultaneous determination of ofloxacin (OFX) and flavoxate hydrochloride (FLX) in pharmaceutical formulations by absorption ratio and second derivative UV spectrophotometry. 20 µg/ml solutions of OFX and FLX were produced separately for the second order spectrophotometric method. The drugs were determined at 311.4 nm which is the zero-crossing for OFX and 246.2 nm which is the zero-crossing for FLX. OLX and FLX showed linearity over the concentration range of 2-30 µg/ml and 2-75 µg/ml, respectively. This method was found to be quick, definite, and exact, and it can be effectively used for rapid screening of OFX and FLX in combination dosage form.

5. Aseel M Aljeboree *et al*., [11], have reported determination of phenylephrine hydrochloride (PHE) and amoxicillin (AMX) in a binary mixture using derivative spectrophotometry methods. They have prepared stock solution for PHE in the concentration range of 2-150 mg/L and for AMX in the concentration range of 2—240 mg/L. PHE and AMX were estimated using the absorbance values of the first derivative spectrum at 228, 258 and 241 nm and the second derivative spectrum at 238, 277 and 226 nm, respectively. By mixing 2-150 mg/L PHE with 0, 20, 100 mg/L AMX and 2-240 mg/L AMX with 0, 20, 100 mg/L PHE, this approach followed beer's law. The analysis of pharmaceutical formulations may easily be done using the stated methodology

6. Dubey S *et al*., [13], have reported a validated method development for estimation of simvastatin by first order derivative spectroscopy. They determined simvastatin by first

order spectrophotometric method using methanol as a solvent and the absorption maximum obtained was 258nm. The results were linear in the concentration range of 10 to 60 µg/ml and also followed beer's law in this range. The correlation coefficient (r^2), limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.999, 1.808 µg and 5.48 µg, respectively. The drug's recovery rate was shown to be 103.39%. The devised UV spectrophotometric approach may be effectively implemented as a substitute for HPLC and HPTLC methods for quantitative determination of simvastatin

7. Vishal Shah *et al*., [14], have reported the development and validation of derivative spectroscopic method for simultaneous estimation of cefixime trihydrate (CEF) and azithromycin dihydrate (AZI) in combined dosage form. To get rid of spectral interferences, they have used second order derivative spectroscopy. AZI and CEF exhibited zero-crossing points in water at 326.4 nm and 226.8 nm, respectively. At concentration ranges of 10-40 ppm for CEF and 25-100 ppm for AZI, the technique complies with beer's law. The correlation coefficient (r^2), LOD and LOQ values obtained for CEF were 0.9992, 0.54 and 1.64 ppm whereas for AZI it was 0.9990, 0.77 and 2.34 ppm, respectively. For the quantitative analysis of a commercially available dosage form (ZIMNIC –AZ), the designed and validated procedure was effectively applied.

8. Pradeep Kumar *et al*., [15], have reported the development and validation of a new spectroscopic method for the estimation of metadoxine (MDL) in bulk and solid dosage form. They have developed a technique where distilled water was used as a solvent for the UV spectroscopic estimation of MDL in both bulk and tablet formulation. For first, second and third order derivative spectroscopy the absorbance was found to be 302 nm, 270 nm, and 314 nm, respectively with the regression values of 0.9965 for 1^{st} order derivatives, 0.9992 for 2^{nd} order derivatives and 0.9996 for 3^{rd} order derivatives. In the concentration range of 4-40 µg/ml, the procedure complies with beer's law. The suggested approach is exact, linear, precise, stable, repeatable, and it can be used to analyse both tablet and bulk forms of the drug metadoxine.

9. Mohammad Mudassar*et al.* [16], have reported UV first order and second order derivative spectrophotometric methods using amplitude and AUC technique for determination of sildenafil in bulk and in pharmaceutical formulation. They have developed 4 methods which are: first order derivative UV spectrophotometry using amplitude (Method A), first order derivative UV spectrophotometry using area under curve technique (Method B), second order derivative UV spectrophotometry using amplitude (Method C), and second order derivative UV spectrophotometry using area under curve technique (Method D). Distilled water was used as the solvent for UV spectroscopic analysis. The amplitude for "Method A" was measured at 313 nm and for "Method C" at 297 nm, whereas the AUC for "Method B"was integrated across the wavelength range of 302-326 nm and for "Method D" in the wavelength range of 281-310 nm. The drug sildenafil followed the Beer's-Lambert Law in the concentration range of 5 to 50 µg/mL for all the 4 methods. It was also observed that the correlation coefficients for all the methods were more than 0.999. These methods are accurate, precise and cost-effective for determination of sildenafil and can be used when sophisticated tools like HPLC are not accessible.

10. I. J. Al-Nuri *et al.* [17], have reported UV derivative spectra for determination of Coenzyme Q_0 (Ubiquinone Q_0). The stock solution was prepared utilizing distilled water as the solvent. For the first order derivative spectrum, the positive peak, the zero-crossing value, and the negative peak were found at the wavelength 230-268 nm, 268 nm, and 268-314 nm, respectively. On plotting calibration curve between integrated area under the positive peak against the molar concentration of pure coenzyme Q_0 solution, it obeyed the Beer's-Lambert rule over the concentration range of 0.1-18.2 µg/ml with an r^2 value of 0.9999, whereas on plotting the calibration curve between integrated area under the negative against the molar concentration of pure coenzyme Q_0 solutions, it obeyed the Beer's lambert law in the range of 0.01-18.2 µg/ml with an r^2 value of 0.9999. For the second order derivative spectrum, a main negative peak was seen at 254-284 nm with two positive peaks on the other sides. A calibration curve was plotted between integrated area under the peak against the molar concentrations which showed linear relationship in the range of 0.02-18.2 µg/ml thereby obeying Beer's-Lambert law with an r^2 value of 0.9999. For the third order derivative spectrum, the negative peak, the zero-crossing value, and the positive peak werefound at the wavelength 222-268 nm, 268 nm, and 268-292 nm, respectively. On plotting calibration curve between integrated area under the negative peak against the molar concentration of pure coenzyme Q_0 solution, it obeyed the Beer's-Lambert rule over the concentration range of 0.002-18.2 µg/ml with an r^2 value of 1.00, whereas on plotting the calibration curve between integrated area under the positive against the molar concentration of pure coenzyme Q_0 solutions, it obeyed the Beer's lambert law in the range of 0.02-18.2 µg/ml with an r^2 value of 0.9999. The designed method is stable, cost-efficient and more reliable when compared to that of HPLC for determination of coenzyme Q_0.

11. D. Madhuri*et al*., [18], have reported spectrophotometric estimation of moxifloxacin (MFX) hydrochloride using osmium (Os-VIII) ions in micellar medium. In aqueous environment, they synthesized chelate between MFX and osmium (Os-VIII). 1st order derivative was seen at 435 nm and the 2nd order derivative at 454 nm, and had an apparent molar absorptivity of $2.1867x10^4$ $L\text{-}M^{-1}Cm^{-1}$. The chelate formed obeyed Beer's-Lambert law over the concentration range of 1 to 10 µg/ml for 1^{st} order derivative whereas 1 to 15 µg/ml for 2^{nd} order derivative. The limit of detection (LOD) and limit of quantification (LOQ) for 1^{st} and 2^{nd} order derivative were 0.27, 0.12 and 0.81, 0.384, respectively with a correlation coefficient (r^2) of 0.999 for 1^{st} order derivative and 0.997 for 2^{nd} order derivative. Percentage recoveries was found to be 100.2±0.1463 for 1^{st} order and 100.3±0.1065 for 2^{nd} order, according to the findings obtained by using this methodology.

12. Mali A*et al*., [19], reported the development and validation of the first order derivative estimation of Ranitidine precisely. Shimadzu 1800 series UV spectrophotometer was used for UV estimation. Ranitidine was given by Cipla pharmaceutical and 125mg tablet form was used. Methanol was used as a solvent which was from Research-Lab Fine Chem Industries. A 10 µg/ml stock solution of ranitidine was prepared and dilutions were made using methanol of about 2, 4, 6, 8 and 10 µg/ml concentrations and scanned from 400 to 200 nm. First order derivative area under the curve ranged from 329-340 nm. Calibration curve of AUC v/s concentration was plotted and the concentrations were found to be

linear with a correlation coefficient of 0.999. The Limit of detection (LOD) value was 0.62 µg/ml and Limit of quantitation (LOQ) was about 1.67 µg/ml. Thus, this study was accurate, precise and effective which enables us to understand the first order derivative of ranitidine using the UV estimation process.

13. Tambe S *et al*., [20], have reported the development and validation of the first order UV spectroscopy in Dorzolamide and Timolol maleate in biological fluid accurately. The dorzolamide and timololwere supplied by Cipla. Standard tear fluid was prepared by dissolving 0.670 g sodium chloride, 0.200 g sodium bicarbonate, and 0.008 g dehydrated calcium chloride in distilled water. Ph was adjusted to 7.4 by HCl. 1 mg/ml stock solutions of dorzolamide and timolol were prepared. Shimadzu 2600 UV spectrophotometer with 2 nm slit width was used in the estimation. So 4 – 28 µg/ml of dorzolamide and 10 – 50 µg/ml of timolol concentration range was prepared. The first order derivative of dorzolamide was measured at 251.80 nm and that of timolol was 295 nm. The concentration range of dorzolamide and timolol i.e., 4-28 µg/ml and 10-50 µg/ml respectively were linear and obeyed Beer-Lambert's law. The LOD value of dorzolamide was found to be 0.040 µg/ml and that of timolol was 0.72 µg/ml. The LOQ values were 0.91 µg/ml and 1.06 µg/ml respectively. Thus, this study concludes with an accurate validation and development process which is effective as well as can be used widely in UV spectroscopy of dorzolamide and timolol.

14. Alkhafaji S *et al*., [21], have reported the development and validation of the first order derivative estimation of Paracetamol, Ibuprofen and Caffeine in bulk as well as pharmaceutical formulation. The all three drugs i.e. paracetamol, ibuprofen and caffeine were supplied by Samarra drug industries. Ethanol and NaOH were supplied by HIMEDIA which were used as solvents. Shimadzu 1800 series with UV probe 2.32 was used in instrumentation. 10 µg/ml ibuprofen, 1.5 µg/ml caffeine and 16.5 µg/ml paracetamol were used in the estimation of the first derivative spectrum. Absorbance was measured at a range of 200 – 400 nm and a calibration curve was plotted. RSD% value was <2 which shows the method was precise. LOQ values were 2.105, 0.987 and 2.097 respectively whereas LOD values of Ibuprofen, Caffeine and Paracetamol were 0.631, 0.2962 and 0.629 respectively. Thus, this study validated the accuracy, precision, RSD%, LOD and LOQ which shows that the study concludes with accurate results which can be used in estimation of first order derivatives of Paracetamol, Caffeine and Ibuprofen.

15. Bhange P *et al*., [22], have reported the development and validation of the first order UV spectroscopy of Cefixime in bulk as well as in pharmaceutical formulation. The cefixime was offered by Ajanta pharma. So 10mg of cefixime was dissolved in a 100 ml volumetric flask containing 25 ml of methanol to produce a stock solution of 100 g/ml. The absorbance was at 230 nm. The standard drug solution was diluted to get concentration in the range of 5-35 g/ml and for first order derivatives the sharp peak or the absorbance was at 238.5 nm. So, the standard drug solution was again diluted to get concentration in the range of 10-50 µg/ml and further scanned for first order derivatives. The dA/d v/s concentration calibration curve was plotted. AUC method was carried out using the 100 mg/ml drug solution and the wavelength was in the range of 400-200 nm and the cefixime tablet formulation was taken crushed, powdered and 100 mg/ml drug

concentration solution was prepared and estimated using calibration curve. So, all the methods were validated according to ICH guidelines. The LOD value was found to be 0.0299 whereas the LOQ value was 0.694. The regression constant r2 value was found to be 0.9994 which shows the study was accurate and precise and can also be used effectively in UV first order estimation of cefixime.

16. Shah R *et al*., [23], have reported the development and validation of the first order UV spectroscopy of Amlodipine besylate and Indapamide using both bulk and pharmaceutical formulation. Amlodipine was gifted by ZydusCadila and Indapamide was gifted by Dishmanpharma. Shimadzu 1800 series UV spectrophotometer was used in the estimation. About 50 mg of both drugs were dissolved in methanol in a 50 ml volumetric flask and also the same methanol was used to make up the volume to get standard stock solution of 100 µg/ml concentration. Standard solution of both drugs was taken i.e. 10 µg/ml and scanned UV range to determine peak. So the absorbance of Amlodipine was at 360 nm whereas indapamide was at 242 nm. A series of concentration was prepared i.e., 10-70 µg/ml for amlodipine and 2-16 µg/ml for indapamide and calibration curves were plotted. Both the drugs obeyed linearity and Beer's-Lambert law. Standard drug solution of each drug was taken and scanned in the range of 400-200 nm. Drugs caused zero crossing at their peak and showed first order derivatives respectively. The RSD% was in the range of 1.24 – 1.28. The LOD value of amlodipine was found to be 0.52 and of indapamide was 1.09. The LOQ values were 0.38 and 0.68 respectively. Thus, this study concludes with accurate and precise results of UV spectroscopy of Amlodipine and Indapamide for first order derivative estimation.

17. Borse J *et al*., [24], have reported the development and validation of the first order derivative UV spectroscopy of Naratriptan Hydrochloride in bulk and formulation. Naratriptan was gifted by USV Ltd. Shimadzu UV series was used in estimation. 10 mg naratriptan was dissolved in 100 ml methanol to produce 100 µg/ml. The series of concentration was prepared of about 10-60 µg/ml and scanned in UV range of 400-200 nm. The first order spectra were estimated and the absorbance was at 232.2 nm. The concentration v/s amplitude of the trough linearity graph was plotted. In the AUC method the AUC between 2 wavelengths was taken i.e., 294.20 – 299 nm and a suitablecalibration curve was plotted. The concentration range 10-60 µg/ml obeyed linearity and also Beer's-Lambert law. The methods were validated using ICH guidelines. The RSD% values were least which indicates the methods used were precise and effective. So thus, the study concludes that the method used here results in accuracy and can be used for estimation of first order derivatives of Naratriptan Hydrochloride.

18. Attimarad Mahesh [25], have reported the development and validation of the first order UV derivative of Ofloxacin and Flavoxate hydrochloride using UV spectrophotometer. Pure Ofloxacin was offered by Micro Labs. Shimadzu 1700 series with UV-probe software was used in instrumentation. The 20 µg/ml solution of both drugs were scanned between 400-200 nm to obtain first order derivatives. The calibration curves were plotted using different concentrations. The absorbance was found to be 303.6 nm and 329.8 nm for ofloxacin and flavoxate respectively and graphs were plotted separately. For ofloxacin 0.5–2.5 µg/ml concentration range was prepared and estimated for first order. So

ofloxacin was determined at 344.6 nm and for flavoxate 0.5-3.0 µg/ml concentration range was prepared and estimated first order which was at 334.2 nm. The methods used were validated according to ICH guidelines. The concentration range i.e. 0.5-3 µg/ml of ofloxacin and 0.5-7 µg/ml of flavoxate were found to be in linearity. The limit of detection (LOD) was found to be 0.28 of ofloxacin and 0.27 of flavoxate. The limit of quantification values was 0.47 and 0.42 respectively which represents that the method used is precise and the correlation coefficient was found to be 0.999. Thus, this study concludes with the results which are accurate, precise and effective to estimate Ofloxacin and Flavoxate for first order derivatives.

19. Schwack W*et al*., [26], have reported the development and validation of the second order UV derivative of Dithiocarbamate residues as methyl xanthine. Perkin-Elmer UV spectrophotometer model 552 was used in the instrumentation with 2 nm slit width. 50 mg CS2 (maneb, mancozeb, metiram, propineb, and zineb) was dissolved in 50 ml methanol in a volumetric flask to prepare the stock solution. Methanol was used to make up the volume to get 1 mg/ml concentration. Further 10 ml was pipetted out from the above solution into 1 L volumetric flask and diluted with methanol to gel 10 µg/ml concentration solution. Further 0.0, 2.5, 5.0, 10.0, 15.0, 20.0, 30.0, 40.0, 50.0, and 60.0 µg CS2 were used in different volumetric flasks and 1.25 M methanolic KOH was mixed up to the mark and UV estimation was carried out. The absorbance was at 302 nm and the second order derivative was determined by scanning the sample between 240–360 nm. The concentration range 0.3–2.4 µg/ml was linear and obeyed beer's law. The coefficient of variation was 1.8%. Thus, the study concludes that the second order UV estimation procedure is cost effective and does not need much solvents and the results were accurate and precise which help in further scientific studies or drug discovery procedure.

20. El-GindyA*et al*., [27], have reported the development and validation of the second order UV derivative of Benazepril hydrochloride and Hydrochlorothiazide in binary mixture. The benazepril and hydrochlorothiazide were supplied by Swiss-pharma. Shimadzu UV 1601 PC series was used in instrumentation. Methanol and hydrochloric acid were used as solvent. So, 100 mg of each drug was dissolved in 100 ml methanol and 0.1 M hydrochloric acid was used to get concentration range 4-20 µg/ml. The first order derivative was recorded in the range of 200 – 280 nm and the second order derivative was measured at 273.2 nm. All three methods which are used in the study are validated according to ICH guidelines. So thus, this study concludes with accurate and precise results in UV estimation of Benazepril hydrochloride and Hydrochlorothiazide which can be considered as effective methods.

21. Tatar S *et al*., [28], have reported the development and validation of second order UV spectroscopy of Valsartan in its formulation. The Valsartan was supplied by Novartis. Shimadzu 1600 series was used in instrumentation and scanned in the UV range 200-400 nm. 6 µg/ml and 2 µg/ml concentration was used using ethanol and estimated second order derivatives. Absorbance maxima was at 205.6 nm and the concentration range of 2-10 µg/ml in ethanol was in linearity. Limit of detection (LOD) was found to be 0.5 µg/ml and Limit of quantification (LOQ) value was 2 µg/ml. The correlation coefficient (r^2) was 0.9997. So thus, this study concludes by saying that the UV second order estimation

method can be used accurately and precisely for further studies effectively. Whereas the HPLC method is said to be time-consuming and needs much more solvents. So the UV method of second order derivative can be used effectively in the estimation.

22. WalilyA*et al*., [29], have reported the development and validation of first order derivative UV spectroscopy, TLC densitometry of Mebeverine hydrochloride and Sulpiride. The mebeverine was supplied by Pharcopharma and the sulpiride was supplied by Memphis pharma. Shimadzu UV 1601 series was used in instrumentation. The first-derivative amplitudes were 214.2 nm and 221.6 nm for mebeverine and sulpiride respectively. The concentration range was 10–30 µg/ml for mebeverine and 2–8 µg/ml for sulpiride. So the drug solutions were scanned between 350–200 nm to estimate first order derivatives using 0.1 M Hydrochloric acid as a blank. So 221.6 nm was absorbance of zero-crossing mebeverine and 214.2 nm was absorbance for zero-crossing sulpiride. So thus to obtain results calibration curves were plotted and the RSD% values were least which indicates that the methods used are precise. The concentration range was linear and the correlation coefficient was about 0.999. Thus the study concludes saying that the methods used here are accurate, precise and can be used in estimation of UV first order derivatives in a very effective manner as they are validated according to ICH guidelines as well.

23. Nagulwar V *et al*., [30], have reported the development and validation of first order derivatives for Ritonavir and Lopinavir in combined dosage form using UV spectroscopy. The drugs Ritonavir and Lopinavir were supplied by Cipla. Shimadzu 1601 series UV spectrophotometer was used in instrumentation. Standard stock solutions of 1 mg/ml of both drugs were prepared using acetonitrile. Series of concentration range were prepared using diluted acetonitrile as 5:20, 10:40, 20:80, 15:60, 25:100 and 30:120 µg/ml respectively. So 20 µg/ml ritonavir solution and 80 µg/ml lopinavir solution was prepared and scanned between 400-200 nm. Ritonavir showed zero crossing at 278.10 nm whereas lopinavir showed at 246.70 nm. Further concentration range drug solutions were prepared i.e. 5-40 µg/ml for ritonavir and 10-120 µg/ml for lopinavir and first order derivative was estimated. Absorbance of ritonavir was at 246.70 nm and of lopinavir was at 278.10 nm. For further analysis calibration curves were plotted. Thus the study concludes with accurate and precise results in estimation of first order derivatives for Ritonavir and Lopinavir in a very effective manner.

24. Dinesh M. Dhumal*et al*., [31], have reported the development and validation of an accurate and precise method by using UV spectrophotometry for Quantitative determination of Moxifloxacin hydrochloride (MOX) in bulk and ophthalmic solution and by first order derivative using area under curve. MOX showed maximum absorbance at 288.2 nm in double RO water. In the concentration range of 2-12 µg/mL ($r2 > 0.99$), MOX follows the linearity in Zero Order and First Order Derivative spectrophotometric methods. Moxifloxacin Hydrochloride of 5mg/mL was used and UV-Visible spectrophotometer (2450 Shimadzu, software UV Probe 2.21) with spectral Bandwidth of 1 nm was used. For the growth of spectral features of MOX, Double Reverse Osmosis (R.O.) water was used. Zero Order and First Order Derivative spectrophotometric methods estimated the amount of MOX which was found to be 99.97±1.21 and

99.86±1.82. Thus this study was accurate, precise and effective which enables us to understand routine estimation of MOX.

25. AudumbarDigambar Mali *et al*., [32], have reported the development validation of an accurate and precise method by the UV – spectrophotometric method for estimation of ampicillin trihydrate in bulk and formulation by first order derivative area under curve. By using the second order Derivative Area under Curve method values, the quantitative determination of the drug was measured to be 224-231 nm. In the concentration range of Ampicillin Trihydrate using 5-25µg/ml (r^2=0.997) for first order Derivative Area under Curve spectrophotometric method, Calibration graphs were constructed at their wavelengths of determination which were linear. For all spectral computation, a shimadzu 1800 UV/VIS double beam spectrophotometer with 1cm matched quartz cells was used. For First Order Derivative Area under Curve spectrophotometric Analysis, a stock solution of 10µg/ml of Ampicillin Trihydrate was made ready in methanol. The concentrations of 5, 10, 15, 20, and 25µg/ml were obtained when the dilutions were made from Standard Stock solution. 0.59µg/ml &1.47µg/m were the Limit of Detection (LOD) and Limit of Quantification (LOQ) of Ampicillin Trihydrate and 0.997 is the r^2 value. 0.0481 is the % RSD used for precision and by recovery studies at three different levels i.e. 80%, 100%, 120%, the accuracy of the method was evaluated. The accuracy of standard deviation is indicated when the % RSD value is ≤ 2. Thus this study is simple, accurate and precise and can be used for assay of bulk drugs and for pharmaceutical dosage formulations.

26. Sacide Altınöz *et al*., [33], have reported the development validation of an accurate and precise by derivative UV- spectrophotometric method for Simultaneous determination of Indigotin and Ponceau-4R in food samples by using Vierordt's method, ratio spectra first order derivative. In the wavelength range of 300-700 nm, first derivative UV spectrophotometric methods and ratio spectra first order derivative were considered. 1.00–50.00 mg/ml and 1.00–52.00 mg/ml were the linearity ranges of Indigotin and Ponceau-4R dyes at UV spectrophotometric methods. The lambda max values in zero Order spectra are 620nm and 507 nm by analyzingVierordt's method. The proposed techniques of determination are accurate, simple, and easy and can be used for the quantitative analysis of binary mixture.

27. Debabrata Ghosh Dastidar*et al*., [34], have reported the development validation of an accurate and precise method by UV spectrophotometry and the study of First-Order Derivative UV -Spectrophotometry Methods for the Estimation of Diazepam in the presence of Tween-20 and Propylene Glycol. The absorbance value of 230 nm and the slope of the tangent of 260 nm were used to build the calibration curves for UV-spectrophotometry and first-order derivative UV-spectrophotometry methods. 230 nm was the wavelength of maximum absorbance of diazepam in phosphate buffer solution. Limit of detection and limit of Quantification were found to be 0.153 µg/ml and 0.389 µg/ml for UV spectrophotometry methods. 0.084 µg/ml and 0.168 µg/ml were the values of parameters of the First order derivative UV-spectrophotometry method. So, the proposed method is simple, rapid, and economical for routine analysis of diazepam in pharmaceutical laboratories.

28. Josilene Chaves Ruela Corrêa *et al*., [35], have reported the development of an accurate and precise method by performance characteristics of high-performance liquid chromatography, first order derivative UV spectrophotometry and bioassay for fluconazole determination in capsules.Preparation of standard and sample solutions are done by chromatographic method, UV method and bioassay. The calibration curve was acquired at five concentration levels of fluconazole solutions for the first order derivative UV method (150-350 µg/mL). The calibration curves for fluconazole showed good linearity over the concentration range from 240 to 1200 µg/mL (r2 = 0.9997). 6.72 µg/mL and 22.41 µg/mL are the limit of detection (LOD)and Limit of Quantification (LOQ) respectively. RSD obtained in the results were 0.82% .The study leads to the conclusion that the methods were simple, cost effective, accurate and easy and can clear any doubts regarding the determination of antimicrobial APIs.

29. Zenon Kokot *et al*., [36], have reported the development of an accurate and precise method by second-derivative UV spectrophotometry for Simultaneous determination of salicylic acid and acetylsalicylic acid in aspirin delayed-release tablet formulation. The Zero-order absorption spectra and second derivative spectra of ASA and SA were catalogued in a diluting solution of Acetonitrile–formic acid (99:1). At 292 nm for determination of ASA and 328 nm for the analysis of SA, the absolute values of the derivative were measured. For salicylic acid, Mean second derivative value of 0.001061 With RSD of 1.56% was acquired and for acetyl salicylic acid, mean 0.001191 with RSD of 1.36% was obtained. A simple UV method for the calculation of Impurities of salicylic acid in aspirin tablet formulations was evolved.

30. Rajan V. Rele *et al*., [37], have reported the development of an accurate and precise method by UV Spectrophotometric Estimation of Carvedilol Hydrochloride by Second Order Derivative Methods in Bulk and Pharmaceutical Dosage Form. At 247.5nm, Carvedilol hydrochloride was roughly calculated for the second order derivative UV-spectrophotometric method. Beer's law was followed in the concentration range of 1 to 14 µg / ml with coefficient of correlation value 0.9999 for second order derivative method. 0.03243 % was the accuracy presented as relative standard deviation. To calculate the absorbance of the solution, Shimadzu UV-1800 was used with a 10 mm matched quartz cell. A 10 µg /ml solution of carvedilol hydrochloride was scanned in the spectrum mode from 300 nm to 200 nm by using absolute alcohol as blank for the picking up of analytical wavelength. By using derivative mode by UV probe 2.42 software, the second order derivative spectrum was obtained. At 247.5 nm, the amplitude of the derivative spectrum was calculated from the spectrum. In the concentration range of 1 to 14 µg/ml, the calibration curve was produced. Limit of detection was found to be 0.07152 µg/ ml and the limit of Quantification was found to be 0.2167 µg/ml. Through derivative mode, the second order derivative spectrum prevailed. Thus, the study leads to the conclusion that the methods are simple, easy to apply, low-cost and require relatively inexpensive instruments.

31. V. Tantishaiyakul *et al*., [38], have reported the development of an accurate and precise method by Simultaneous determination of dextromethorphan HBr and bromhexineHCl in

tablets by first-derivative spectrophotometry. Correlation coefficients of 0.9999 was obtained for both the analytes and the calibration graph were linear. The limit of detection was 0.033 for dextromethorphan HBr and 0.103 mg. By using a Hewlett–Packard 8452A diode-array spectrophotometer, using a 1 cm quartz cell, spectrophotometric Analysis was done and for the calculation of the derivative spectrum, aSavitsky–Golay polynomial fitting with a polynomial degree of three were handled. The preparation of solutions of dextromethorphan HBr (600 μg /ml) andbromhexineHCl (300 μg/ml was done by liquefying the compounds in methanol. A 25.0 ml part of each solution was moved into a 50 ml volumetric flask and diluted to volume with phosphate buffer solution (pH 6) for UV Quantification which consists of KH_2PO_4 (0.5 M)–NaOH (0.5 M)–H2O (12.5:1.4:36.1, v/v/v), to get the solutions of dextromethorphan HBr (300 μg /ml) and bromhexineHCl (150 μg /ml). The UV spectra of working standard and sample solutions were set down against 50% methanol in phosphate buffer solution (pH 6) as a blank. The concentration ranges of dextromethorphanHBr and bromhexineHCl were 24.0–120.0 mg/ml and 12.0–60.0 mg/mlrespectively. The study leads to the conclusion that the methods are simple, rapid and shows good accuracy and precision.

32. AkgülYesilada *et al*., [39], have reported the development of an accurate and precise method by Second Derivative spectrophotometric Determination of p-Aminophenol in the presence of Paracetamol. At 223.8 nm , second derivative absorbance values were calculated where p-aminophenol showed derivative feedback obeying Beer's Law but paracetamol had negligible derivative absorption .The concentrations of p-aminophenol solutions produced in 0.1 N HC1 (0.12-7.61 mcg/ml) having constant amounts of paracetamol (20 mcg/ml) connected linearly with the d2A/dA2 values and hence gave a straight line (r = -0.9999). By using a Shimadzu Uv-160A Recording Spectrophotometer with a spectral slit width 2nm, Second derivative UV spectra were recorded in 1-cm quartz cells at wavelength range 295-200 nm. The speed of the scan was fast at 2400 nm/min and the response obtained was at 0.02 sec and 60 sec is the cycle time. 12 dilutions were prepared from paracetamol solution at a concentration range of 0-32 mcg/ml and add 1.6 ml from p - aminophenol stock solution to each solution before dilution and complete to volume and compute the d2 values. P-aminophenol Solutions containing paracetamol have Second derivative absorbance values and which show proportional relationship with p - aminophenol with a correlation coefficient of -0.9999. At a concentration level of 0.95 mcg/ml and relative standard deviation of 0.99% (n=6), the precision of the method was examined. The results lead to a conclusion that this method is rapid, precise and accurate.

33. Namita Kapoor *et al.* [40], have reported the development of an accurate and precise method by first derivative spectrophotometry and high-performance liquid chromatography for simultaneous determination of lamivudine and stavudine in antiretroviral fixed dose combinations. Using Beckman UV-spectrophotometer 640i, using a 1 cm quartz cell, spectrophotometric scanning was done. With the instrument setting of first derivative mode with 17 smoothing points and at scan rate of 1200 nm/min in the range of200–350 nm.Stock solution was produced separately in 0.1 N Hydrochloric acid to get a concentration of 1 mg/ml of both drugs, which were later mixed to get a mixture containing 500 μg / ml of both the drugs. In the concentration range of 2–

14µg/ml of stavudine and 2–20 µg/ml for lamivudine against 0.1 N HCl as blank, calibration curves were prepared .Lamivudine is assessed at 300 nm where the dA/dλ value of Stavudine approaches zero; similarly stavudine is assessed at 280 nm where the dA/dλ value of lamivudine is unimportant .The recoveries fluctuated from 99.8 to 102.2% for lamivudine and 100.9–102.6% for stavudine. The six-point calibration curves that were built was linear over the picked concentration range for both drugs (R2 > 0.999). From 99 to 102% , the accuracy of the both drugs were present .LOD and LOQ for lamivudine was established to be 0.13 and 0.40µg,respectively and for Stavudine the values were 0.14 and 0.44 µg/ml individually. Hence the study leads to the conclusion that the methods showed good linearity, precision and reproducibility.

34. JelenaParojcia *et al.*, [41], have reported the development of an accurate and precise method by Second-order Derivative UV Spectrophotometric Method for the Direct Determination of Paracetamol in Urine Intended for Biopharmaceutical Characterisation of Drug Products. The techniques used for calculation of paracetamol in biological fluids are HPLC and spectrophotometric determinations. On a GBC 914 spectrophotometer (GBC Scientific Equipment Pty Ltd, Dandenong, Australia), UV absorption spectra were documented. Scan Speed of 60 nm/min, slit width of 2 nm and a wavelength step of 0.21 nm are the instrument parameters which are followed. 5.0 nm Is the derivative spectrum found. 5.0–30.0 µg/ml is the concentration range of a standard solution. By using 2.0 mg/ml paracetamol aqueous solution, the limit of detection was experimentally insistent on. From the healthy volunteers, the urine samples were collected which were diluted 1:100. In the wavelength range of 220-400 nm, the zero-order spectra of all examined samples were recorded against water. The zero-order absorption spectra of paracetamol in water shows maximum absorbance at 243 nm, where as in the second derivative spectra, a Broad minimum peak at 244–248 nm was acquired under explained experimental conditions And selected set of instrumental framework . 0.9995 is the correlation coefficient of the calibration curve. For the solution of paracetamol containing 3.5 mg/ml, repeatability of the proposed method was examined and 1.62% is the relative standard deviation (RSD). The limit of detection (LOD) was found to be 3.47 µg/ ml and the limit of Quantification (LOQ) was found to be 3.5 µg /ml. Hence the study leads to the conclusion that the methods are simple, accurate, non- encroaching and cost effective.

35. Rajan V Rele *et al.*, [42], have reported the development of an accurate and precise method by UV spectrophotometric estimation of rupatadinefumarate by first order derivative and area under curve methods in bulk and pharmaceutical dosage form. All spectral absorbance Quantifications were made on Shimadzu UV-1800 with 10 mm matched cell. In a volumetric flask of 100 ml , 10 mg of standard rupatadinefumarate was weighed precisely and for about 15 min , 30 ml of absolute alcohol was added and Sonicated for 15 min . To give concentration as 100 µg/ml , the volume was altered up to the Mark with up to the Mark with absolute alcohol .10 µg /ml solution of rupatadinefumarate was examined in the spectrum range of 300-200 nm, for the selection of analytical wavelength. By using UV probe 2.42 software, the first order derivative spectrum was procured. In between 210 – 220 nm, it is the quantification of amplitude of the derivative spectrum. By using UV probe 2.42 software, the area under the curve between λ1 and λ2 was deliberated. In the spectrum mode of 300-200 nm, 10 µg/ml

solution of rupatadinefumarate was scanned. AUC computation was done from the zero Order spectrum and between 245-255 nm, the AUC spectrum was calculated. On the basis of recovery studies, accuracy of the proposed methods were done and by carrying out the analysis of homogeneous powder blend of tablets, the method precision was entrenched. Limit of detection of first order derivative method and AUC method are 0.5999 and 0.1686 µg/ml and the limit of Quantification of first order derivative method and AUC method are 1.815µg/ml and 0.5122 µg/ml respectively. Thus this study leads to the conclusion that the methods are simple, accurate, and rapid.

Conclusions

In the current review study of first and second order derivative estimation of many drugs using UV spectroscopy concludes that the results obtained in all studies were up to the mark and were accurate which can help us in further studies or research purposes. The UV method used here is very effective and easy with cost effectiveness and does not require much solvents, chemicals and apparatus. The accuracy, precision, RSD%, LOD, LOQ estimation, the assay procedure, plotting calibration graphs, etc. were developed and validated according to ICH guidelines itself. Thus the review concludes that the methods used in the study are very accurate and the results were precise can be implemented in our study as these were validated according to ICH using UV spectrophotometer with different drugs as mentioned.

Author Contributions

Shazia Mulla and Nikhil Gawas: writing- original draft, writing- review and editing. **Shreyas Kulkarni, Shankar Gharge and Sagar Y Patil:** writing-review and editing. **Sushmita I Hiremath and Mahesh S Palled:** Supervision.

Acknowledgements

The authors are very grateful to Principal Dr. AHM ViswanathaSwamy for his immense support and valuable guidance. Authors are also thankful to the department of pharmaceutical chemistry.

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