ISSN : 0974-7419 Volume 16 Issue 4

Analytical CHEMISTRY
An Indian Journal

Full Paper

ACAIJ, 16(4) 2016 [163-172]

# Five spectrophotometric methods for determination of sulpride in pure form and pharmaceutical dosage form

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## ABSTRACT

Five Simple, rapid, sensitive, accurate and precise stability-indicating spectrophotometric methods were developed for the determination of sulpride in bulk powder and in pharmaceutical preparation. Method (A) First derivative method($^1$D), Method (B) Ratio derivative method($^1$DD), Method (C) Ratio difference method, Method (D) Bivariate method and Method (E) Dual wavelength method are used for the determination of intact sulpride in presence of its degradation product. The methods were validated and successfully applied to the determination of Dogmatil ® 50mg tablets. The obtained results were statistically compared with those of the reported method by applying t-test and F-test at 95% confidence level and no significant difference was observed regarding accuracy and precision. 

## KEYWORDS

Sulpride;
First derivative;
Ratio derivative;
Ratio difference;
Bivariate;
Dual wavelength.

## INTRODUCTION

Sulpride (SLP); 2-methoxy-N-((1-propylpyrrolidin-2-yl) methyl)-5-sulphamoyl benzamide (Figure 1) is the most widely prescribed anti-psychotic drug. It is a selective dopamine D2 antagonist with antidepressant activities[1]. It has found widespread clinical applications for the treatment of acute and chronic schizophrenia as well as similar mental disorders such as hallucination. The British Pharmacopoeia (BP) recommended non-aqueous titration method for the determination of SLP in its pure form, using perchloric acid as a titrant and glacial acetic acid as a solvent. For its dosage forms, the BP recommended a spectrophotometric method based on measuring its absorbance in 0.1 M NaOH at 291 nm[2]. A review of the literature revealed that several analytical methods have been described for the determination of sulpride in pharmaceuticals or biological fluids, including spectrophotometric[3–6], fluorimetric[7,8], chromatographic[9–14], electrophoretic[15-17], voltammetric[18] and chemiluminometric[19]

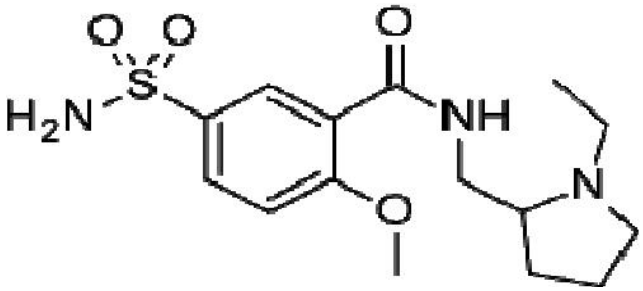


**Figure 1 : Structural formula of sulpride**

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## MATERIALS AND METHODS

### Apparatus

Shimadzu UV-Vis. 1650 Spectrophotometer (Japan).

Hot plate (Torrey pines Scientific, USA).

Jenway, pH meter 3510 (USA).

Rotary evaporator (scilogex, USA)

### Materials and reagents

Sulpride powder was kindly supplied by Ramida (The Tenth of Ramadan) Co. for Pharmaceutical Industries & Diagnostic Reagents, 6th of October City, Egypt.(Batch. NO.A0967911).

Dogmatil ® Tablets. The product of Sanofi aventis Company, Cairo, Egypt. (Batch. NO.4EG025), which labeled to contain 50 mg sulpride per tablet.

Hydrochloric acid, Sodium hydroxide and Methanol (El-Nasr Co., Egypt).

### Standard solution

A stock solution of sulpride (1 mg/ml) was prepared by dissolving 100 mg of sulpride in 50 ml of methanol and complete to 100 ml with methanol and was further diluted with the same solvent as appropriate.

### Degraded sample[8]

Alkaline-induced forced degradation was performed by adding 100 mg of sulpride to 100 mL 4 M NaOH and refluxing at 80°C for approximately four hours. The solution was then left to reach ambient temperature, neutralized to pH 7 by addition of 4 M HCl, evaporated to dryness, the residue was extracted three times with 25 ml methanol,filtered into 100 ml volumetric flask then the volume was adjusted by the same solvent.The obtained solution was claimed to contain (1 mg $ml^{-1}$).

## PROCEDURE

### Construction of the calibration curves (general procedures)

### Method A (first derivative method)

Aliquots of standard sulpride solution in methanol (1 mg $ml^{-1}$) containing (0.1 – 1.5) mg of the drug were added to a series of 10- ml volumetric flasks and then diluted to the mark with methanol. First - derivative ($^1D$) spectra of the drug were recorded against methanol as blank. The amplitude of the trough at 280.4 nm was measured for each drug concentration.

A Calibration curve relating trough amplitude to drug concentration in μg $ml^{-1}$ was constructed, the regression equation was derived.

### Method B (ratio derivative method)

Aliquots equivalent to(0.1 – 1.5 mg) sulpride and(0.1–1.5mg) sulpride degradate are accurately transferred from their standard working solutions (1 mg $ml^{-1}$) into two separate series of 10- ml volumetric flasks then completed to volume with methanol. The spectra of the prepared standard solutions are scanned from 200 - 400 nm and stored in the computer. For the determination of sulpride in presence of its degradation product, the stored spectra of sulpride are divided by the spectrum of 100 μg $ml^{-1}$ degradate, smoothed with $\Delta\lambda$ = 2 nm and scaling factor = 1, then the first derivative of the ratio spectra ($^1DD$) with $\Delta\lambda$ = 2 nm is obtained. The amplitude of the first derivative trough of (sulpride / degradate) is measured at 296.4 nm.

A calibration graph relating the trough amplitude at 296.4 nm to the corresponding concentrations in μg $ml^{-1}$of sulpride is constructed alternatively, the regression equation was derived.

### Method C (ratio difference method)

Aliquots equivalent to (0.1 – 1.5 mg) were accurately transferred from sulpride standard stock solution (1 mg $ml^{-1}$) into a series of 10- ml volumetric flasks then completed to volume with methanol. The spectra of the prepared standard solutions are scanned from 200 - 400 nm and stored in the computer, For the determination of sulpride in presence of its degradation product, the stored spectra of sulpride are divided by the spectrum of (100 μg $ml^{-1}$) of the alkaline degradate. The amplitude difference at 262.0 and 301.0 nm ($\Delta$262.0 – 301.0) was plotted against the corresponding sulpride concentration in μg $ml^{-1}$ and the regression equation was

computed.

**Method D (bivariate method)**

Different aliquots equivalent to (0.1–1.5) mg of Sulpride and (0.1–1.5) mg of its alkaline degradate were accurately transferred from their standard solutions (1 mg/ ml) into two separate series of 10-ml volumetric flasks and completed to volume with methanol. The absorption spectra (from 200 to 400 nm) of these solutions were recorded using methanol as a blank. The absorbance was measured at 260 and 290 nm and then the corresponding regression equations were computed at the selected wavelengths for both Sulpride and its degradation product.

**Method E (Dual wavelength method)**

Aliquots of standard sulpride solution in methanol (1 mg $ml^{-1}$) containing (0.1 – 1.5) mg of the drug were added to a series of 10- ml volumetric flasks and then diluted to the mark with methanol. The utility of dual wavelength data processing program is to calculate the unknown concentration of a component of interest present in a mixture containing sulpride and alkaline degradate interfering component by the mechanism of the absorbance difference between two points on the mixture spectra. This is directly proportional to the concentration of the component of interest, independent of the interfering components. From the overlay of two drugs for estimation of sulpride, two wavelengths selected (269 nm and 280 nm) where the sulpride degradation shows same absorbance. Eight working standard solutions having concentrations 10, 20, 30, 40, 50, 90, 120 and 150 µg $ml^{-1}$ of the drug were prepared separately in methanol and the absorbance at 269 nm and 280 nm were measured and absorptive coefficients were calculated using calibration curve.

**Analysis of pharmaceutical preparation**

Ten Dogmatil ® 50mg Tablets were accurately weighed and finely powdered, then a quantity equivalent to 100 mg of sulpride was shaken three times with 25 ml methanol for 15 minutes then filtered into 100 ml volumetric flask and the volume was adjusted to the mark with water to obtain a concentration of (1 mg $ml^{-1}$). The solution was analyzed using the procedure described under method A,B,C,D and E.

## RESULTS AND DISCUSSION

**Spectral characteristics**

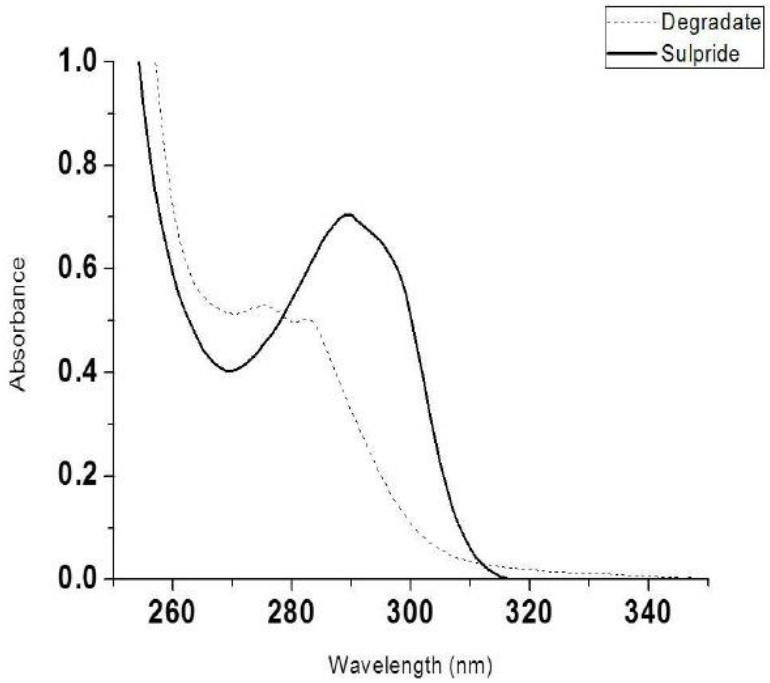


**Figure 2 : Zero-order absorption spectra of intact sulpride (100µg $ml^{-1}$) (—)AND its degradation product (100 µg $ml^{-1}$) (…..) in methanol**

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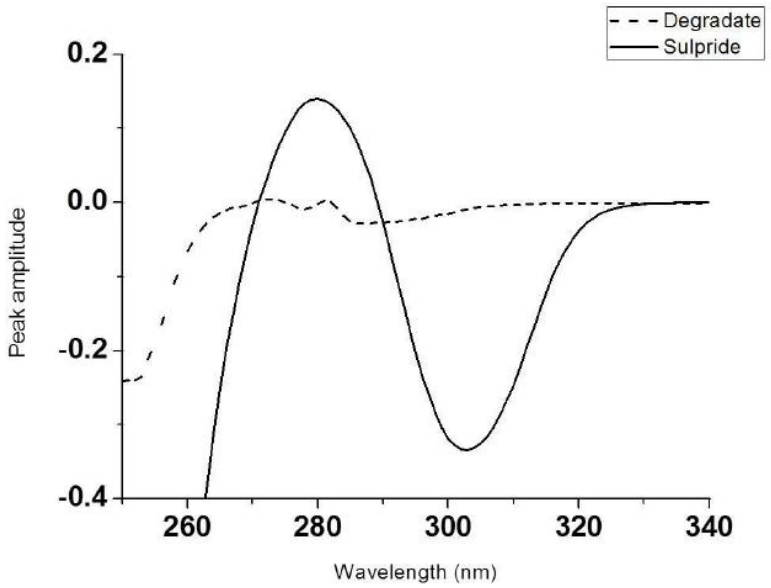


**Figure 3 : First-derivative spectra of intact sulpride (100 µg ml$^{-1}$) (—) and its degradation product (100 µg ml$^{-1}$) (…..) in methanol**

The zero order ($D_0$) absorption spectra of sulpride (100 µg ml$^{-1}$) and its alkaline degradation product (100 µg ml$^{-1}$) were recorded against methanol as blank over the range of 200 – 400 nm (Figure 2).

**For method A**

It is clear from the spectra in (Figure 2) that, there is a band overlapping between the drug and its degradation product. Such overlapping was eliminated by the first derivative ($^1$D) scanning of sulpride and its degradation product in methanol, sulpride has a trough at 280.4 nm which shows no interference from the degradation product. Thus it would be possible to adopt the ($^1$D) spectrophotometry at 280.4 nm for direct determination of sulpride in presence of its degradation product as seen in (Figure 3).

**For method B**

Salinas et al.[20] designed a spectrophotometric method, which is based on the derivation of the ratio-spectra for resolving binary mixtures. The main advantage of the ratio-spectra derivative spectrophotometry is the chance of doing easy measurements in correspondence of peaks so it permits the use of the wavelength of highest value of analytical signals (a maximum or a minimum)[21-23]. Moreover, the presence of a lot of maxima and minima is another advantage by the fact that these wavelengths give an opportunity for the determination of active compounds in the presence of other compounds and excipients which possibly interfere the assay. In this method the absorption spectrum of the mixture (absorbance at each wavelength) is divided by the absorption spectrum of a standard solution of one of the components, and the first derivative of the ratio spectrum is obtained. The concentration of the other component is then determined from a calibration graph.

The main parameters that affect the shape of the ratio spectra are wavelength, scanning speed, the concentration of the standard solution used as a divisor; the wavelength increment over which the derivative is obtained ($\Delta\lambda$) and the smoothing function are carefully tested. The ratio spectra presented in (Figure 4) and the first derivative of the ratio spectra presented in (Figure 5) may provide a good proof for this understanding. The effect of wavelength scanning speed is studied. It is found that at high speed noisy spectra are obtained while at low scanning speed, the noise is decreased but a longer time is needed for the measurements, so medium scanning speed is chosen to perform measurements. Effect of divisor concentration is also tested, different concentrations of divisor are used (60,80 and 100 µg ml$^{-1}$) of sulpride degradate and the divisor of con-

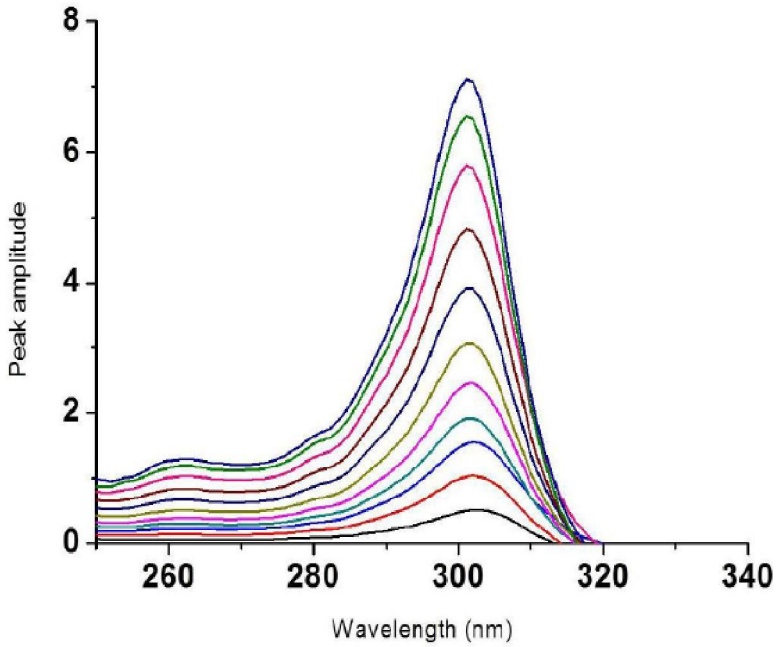


**Figure 4 : Smoothed ratio spectra of sulpride (10-150µgml$^{-1}$) using (100 µgml$^{-1}$) sulpride degradate as divisor and methanol as blank**

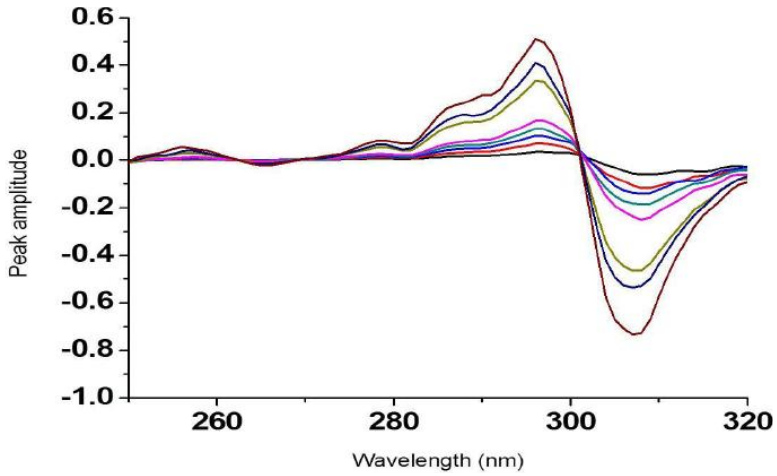


**Figure 5 : First derivative of smoothed ratio spectra of sulpride (10– 150) µg ml$^{-1}$) using (100 µgml$^{-1}$) sulpride degradate as divisor and methanol as blank**

centration 100 µg ml$^{-1}$of sulpride degradate is found the best regarding average recovery percent when it is used for the prediction of sulpride concentrations in bulk powder as well as in laboratory prepared mixtures.

The absorption spectra of sulpride are divided by the absorption spectrum of 100 µg ml$^{-1}$ sulpride degradate and smoothed (Figure 4) for determination of sulpride in the presence of its degradate. This gave the best compromise in terms of sensitivity, repeatability and signals to noise ratio. The choice of wavelength for the measurement was carefully studied. The trough amplitude at 285.0 and 308.0 nm and peak amplitude at 296.4 nm of the first derivative of ratio spectra are then recorded respectively. Good linearity was observed but the recovery percent at 296.4.0 nm was better, which may be attributed to its higher signal to noise ratio.

**For method C**

Ratio difference[24] is a new simple, rapid, selective method for the simultaneous determination of components having overlapping spectra in binary mixtures, having the advantages of minimal data processing and wider range of application. The binary

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mixture of sulpride and its alkaline degradation product was chosen as an example for the application of the new ratio difference method.

The absorption spectra of sulpride and its degradate show a degree of interference as shown in (Figure 2), that the application of direct spectrophotometry failed to determine sulpride in the presence of its degradate.

Several approaches have been developed to remove the overlapping constant in the ratio spectrum, either using certain order derivative or through a sophisticated subtraction followed by multiplication procedure[25], the later was capable of determining only the component with the less extended spectrum in the mixture. The ratio difference method is a simple innovative method was capable of determining sulpride in presence of its alkaline degradate with minimal data processing, high selectivity regardless which component has more extended spectrum.

The method comprises two critical steps, the first is the choice of the divisor, and the selected divisor should compromise between minimal noise and maximum sensitivity. Different concentrations of divisors are used (60, 80 and 100µg $ml^{-1}$) of the degradate and the divisor concentration 100 µg $ml^{-1}$ was found the best regarding average recovery percent when it was used for the prediction of sulpride concentration in bulk powder as well as in laboratory prepared mixtures.

The second critical step is the choice of the wavelengths at which measurements are recorded. Any two wavelengths can be chosen provided that they exhibit different amplitudes in the ratio spectrum and a good linearity is present at each wavelength individually. Linear correlation was obtained between the differences in amplitudes at 262.0 and 301.0nm, against the corresponding concentration of sulpride. Good linearity is obtained in the concentration range of 10 - 150 µg $ml^{-1}$ sulpride.

**For method D**

Bivariate calibration spectrophotometric method is a direct method which has been proposed for the resolution of binary mixtures. The principle of bivariate calibration is the measurement of two components (A and B) at two selected wavelengths ($\lambda_1$ and $\lambda_2$) to obtain two equations

**AAB1 = mA1CACB + eAB1** **(1)**

**AAB2 = mA2CACB + eAB2** **(2)**

The resolution of each equation set allows the evaluation of CA and CB values according to the previously mentioned equations. This simple mathematic algorithm allows the resolution of the two components by measuring the absorbance of their mixture at the two selected wavelengths and using the parameters of the linear regression functions evaluated individually for each component at the same wavelengths. In order to apply the bivariate method in the resolution of sulpride in mixture with its alkaline degradate, the absorbance of the two components at several different selected wavelengths was recorded in the region of overlapping; from 260 to 290 nm at 5 nm interval. The calibration curve equations and their respective linear regression coefficients were obtained directly with the aim of ensuring that there was a linear relationship between the absorbance and the corresponding concentration. All of the calibration curves at the selected wavelengths showed a satisfactory linear regression coefficient ($r^2$> 0.9988). According to Kaiser

**TABLE 1 : Values of the sensitivity matrix determinates calculated according to Kaiser's method (k x $10^{-6}$) for the mixture of Sulpride and Sulpride degradate by the proposed bivariate method**

| λ/λ | 260 | 265 | 270 | 275 | 280 | 285 | 290 |
|---|---|---|---|---|---|---|---|
| 260 | 0 | -0.11 | 0.77 | -0.73 | -0.6.2 | -13.81 | -21.51 |
| 265 | | 0 | 0.66 | -0.47 | -4.61 | -10.35 | -16.18 |
| 270 | | | 0 | -1.09 | -4.99 | -10.81 | -15.8 |
| 275 | | | | 0 | -4.06 | -9.68 | -15.47 |
| 280 | | | | | 0 | -5.54 | -11.97 |
| 285 | | | | | | 0 | -7.43 |
| 290 | | | | | | | 0 |

Method[26], the slope values of the linear regression equations for both Sulpride and Sulpride degradate at the selected wavelengths were used to calculate the sensitivity matrices K to find out the optimum pair of wavelength at which the binary mixtures were recorded as shown in TABLE (1).

$$K = \begin{bmatrix} m_{A_1} & m_{B_1} \\ m_{A_2} & m_{B_2} \end{bmatrix}$$

For the bivariate determination of Sulpride in mixture with its alkaline degradate. 260and 290 nm were found to give the maximum value of K and thus can be used for the analysis; Figure (2). The yielded statistical results are summarized in TABLE (2)

**For method E**

The utility of dual wavelength[27] method is to calculate the unknown concentration of a component of interest present in a mixture containing both the components of interest and an unwanted interfering component by the mechanism of the absorbance difference between two points on the mixture spectra where the absorbance for alkaline degradate was equal at the selected two wavelengths. The calibration curves were prepared at absorbance difference of two wavelengths (269 nm – 280 nm). The response for the sulpride was found to be linear in the concentration range 10 - 150 µg/ml and at absorbance difference of two wavelengths (269 nm – 280 nm). The linearity of the calibration curve was validated by the high values of correlation coefficient, figure (2).

## VALIDATION OF THE METHODS

**Linearity**

**Method A**

At the described wavelength linear relationship was obtained between the trough amplitude and the sulpride concentration in the range (10 - 150µg $ml^{-1}$). The linear regression equation of the trough was:

$$\mathbf{A_{280.4} = 0.0013\ C + 0.0056\ (r = 0.9998)}$$

Where A is a trough height at 280.4 in cm and C is the drug concentration in µg $ml^{-1}$.

**Method B**

Under the described experimental conditions, the calibration graph for the method was constructed by plotting trough height versus concentration in µg/ml. The regression plot was found to be linear over the range of 10-150µg/ml. The linear regression equation for the graph is:

$$\mathbf{P_{296.4\ nm} = 0.0034\ C + 0.0012\ (r = 0.9999)}$$

Where C is the concentration of sulpride in µg $ml^{-1}$, P is the trough height of the first derivative of the ratio spectrum curve at 296.4 nm and r is the correlation coefficient.

**Method C**

Linear correlation was obtained between the differences in amplitudes at 262.0 and 301.0nm, against the corresponding concentration of sulpride. Good linearity is obtained in the concentration range of 10 - 150 µg $ml^{-1}$. The corresponding regression equation was computed to be:

$$\mathbf{\Delta P_{262.0\ -\ 301.0} = 0.0384\ C + 0.1214\ (r = 0.9997)}$$

Where ΔP is the amplitude difference at the selected wavelengths, C is the concentration in µg $ml^{-1}$ and r = the correlation coefficient.

**Method D**

At the described wavelength linear relationship was obtained between the trough amplitude and the corresponding concentration of sulpride. Good linearity is obtained in the concentration range of (10 - 150 µg $ml^{-1}$) sulpride. The corresponding regression equation was computed to be:

$$\mathbf{A_{290} = 0.0071\ C - 0.0059\ (r = 0.9999)}$$

Where A is the peak amplitude at 290nm, C is the concentration in µg $ml^{-1}$ and r = the correlation coefficient, as shown in (TABLE 2).

**Method E**

The calibration curves were plotted over a concentration range of 10 - 150 µg/ml for sulpride.

$$\mathbf{\Delta P_{269.0\ -\ 280.0} = 0.0013\ C + 0.0068\ (r = 0.9997)}$$

Where ΔP is the amplitude difference at the selected wavelengths, C is the concentration in µg $ml^{-1}$ and r

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= the correlation coefficient.

## Sensitivity

The limit of detection (LOD) and the limit of quantitation (LOQ) were calculated according to ICH $Q_2$ Recommendation[28] from the following equations:

**LOD = 3.3 $S_a$ / slope**

**LOQ = 10 $S_a$ / slope**

Where $S_a$ is the standard deviation of the intercept of regression line. LOD was found to be 1.1633, 3.0958, 1.4527, 2.6570 and 1.3026 µg/ml, while LOQ was found to be 3.5251, 9.3811, 4.4022, 8.0516 and 3.9474 µg/ml for method A,B,C,D and E respectively. The small values of LOD and LOQ indicate good sensitivity.

## Accuracy and precision

Three replicate determinations of three different concentrations of sulpride in pure form within linearity range were performed in the same day (intra-day) and in three successive days (inter-day). Accuracy as recovery percent (R%) and precision as percentage relative standard deviation (RSD%) were calculated and results are listed in (TABLE 3). The small values of RSD% indicate high precision of the method. Morever, the good R% confirms excellent accuracy.

## SPECIFICITY

The specificity of the proposed methods was assured by applying the laboratory prepared mixtures of the intact drug together with its degradation product. The proposed methods were adopted for the specific determination of intact sulpride in presence of up to 70 % of its corresponding degradates for the five methods.

**TABLE 2 : Spectral data for determination of sulpride by the proposed methods**

| Parameters | First derivative | Ratio derivative | Ratio difference | Bivariate | Dual wavelength |
|---|---|---|---|---|---|
| $\lambda_{max}$ (nm) | 280.4 | 296.4 | 262.0-301.0 | 290 | 269.0-280.0 |
| Linearity range (µgml$^{-1}$) | 10-150 | 10-150 | 10-150 | 10-150 | 10-150 |
| LOD (µgml$^{-1}$) | 1.1633 | 3.0958 | 1.4527 | 2.6570 | 1.3026 |
| LOQ (µgml$^{-1}$) | 3.5251 | 9.3811 | 4.4022 | 8.0516 | 3.9474 |
| Regression equation* | | | | | |
| Slope (*b*) | 0.0013 | 0.0034 | 0.0384 | 0.0071 | 0.0013 |
| Intercept (*a*) | 0.0056 | 0.0012 | 0.1214 | 0.0059 | 0.0062 |
| Correlation Coefficient (*r*) | 0.9998 | 0.9999 | 0.9997 | 0.9999 | 0.9997 |

**TABLE 3 : Intra-day and inter-days accuracy and precision for the determination of sulpride by the proposed methods**

| | | Intra-day | | Inter-day | |
|---|---|---|---|---|---|
| | Conc. µg.ml$^{-1}$ | Accuracy (R %) | Precision (RSD %) | Accuracy (R %) | Precision (RSD %) |
| Method A | 40 | 101.73 | 0.189 | 100.70 | 1.271 |
| | 90 | 99.68 | 0.916 | 99.20 | 0.504 |
| | 125 | 99.85 | 0.572 | 100.84 | 0.805 |
| Method B | 40 | 99.60 | 1.233 | 99.43 | 0.541 |
| | 90 | 99.35 | 1.594 | 100.18 | 0.506 |
| | 125 | 98.80 | 0.394 | 99.27 | 0.146 |
| Method C | 40 | 100.23 | 0.813 | 98.88 | 0.423 |
| | 90 | 99.86 | 0.406 | 99.88 | 1.406 |
| | 125 | 100.76 | 0.537 | 99.06 | 1.087 |
| Method D | 40 | 98.90 | 0.941 | 98.55 | 1.0718 |
| | 90 | 101.60 | 0.583 | 99.98 | 0.156 |
| | 125 | 99.21 | 1.615 | 99.48 | 1.668 |
| Method E | 40 | 98.65 | 0.515 | 98.71 | 0.490 |
| | 90 | 99.65 | 1.347 | 99.51 | 0.517 |
| | 125 | 100.06 | 0.563 | 100.14 | 0.698 |

**TABLE 4 : Determination of sulpride in mixtures with its degradation product by the proposed methods**

| Intact | Degradate | Degradate | Recovery% of Intact | | | |
|---|---|---|---|---|---|---|
| (µg ml$^{-1}$) | (µg ml$^{-1}$) | % | First derivative | Ratio derivative | Ratio difference | Bivariate |
| 135 | 15 | 10 | 100.63 | 100.65 | 101.06 | 98.55 |
| 130 | 20 | 13.33 | 100.41 | 99.43 | 99.94 | 98.87 |
| 110 | 40 | 26.67 | 101.26 | 101.15 | 99.44 | 100.95 |
| 95 | 55 | 36.67 | 100.73 | 101.42 | 101.13 | 99.24 |
| 45 | 105 | 70 | 99.83 | 98.82 | 100.03 | 99.40 |
| Mean ± SD | | | 100.57±0.518 | 100.30±1.122 | 100.32±0.744 | 99.4+0.924 |

| Intact | Degradate | Degradate % | Recovery% of Intact |
|---|---|---|---|
| (µg ml$^{-1}$) | (µg ml$^{-1}$) | | Dual wavelength |
| 135 | 15 | 10 | 98.46 |
| 130 | 20 | 13.33 | 100.36 |
| 110 | 40 | 26.67 | 101.32 |
| 95 | 55 | 36.67 | 100.24 |
| 45 | 105 | 70 | 98.80 |
| Mean ± SD | | | 99.83 ±1.185 |

**TABLE 5 : Determination of sulpride in dogmatil ® 50mg tablets by the proposed and reported methods**

| Parameters | First derivative | First derivative ratio | Proposed Methods Ratio Difference | Bivariate | Dual Wavelength | Reported*** method[8] |
|---|---|---|---|---|---|---|
| *N** | 5 | 5 | 5 | 5 | 5 | 5 |
| $\bar{X}$ | 100.56 | 100.07 | 98.22 | 99.96 | 99.05 | 99.83 |
| *SD* | 1.287 | 1.886 | 1.414 | 1.170 | 0.738 | 1.11 |
| *RSD%* | 1.280 | 1.0885 | 1.440 | 1.170 | 0.745 | 1.120 |
| *t*** | 2.14 (2.306) | 1.029 (2.306) | 0.673 (2.306) | 1.337 (2.306) | 0.1799 (2.306) | ____ |
| F** | 3.0589 (6.388) | 3.570 (6.388) | 3.693 (6.388) | 2.528 (6.388) | 1.005 (6.388) | ____ |

*** No. of experimental; ** The values in the parenthesis are tabulated values of t and F at (p= 0.05); ***The reported method method**

The percentage recovery ±SD% was 100.57 ± 0.518, 100.3±1.122, 100.32±0.744, 99.40±0.924 and 99.83±1.185 for method A, B, C, D and E respectively, as shown in (TABLE 4)

## PHARMACEUTICAL APPLICATIONS

The proposed methods were applied to the determination of the studied drug in its tablet preparation. The results were validated by comparison to a previously reported method[8]. No significant difference was found by applying t-test and F-test at 95% confidence level, indicating good accuracy and precision of the proposed method for the analysis of the studied drug in its pharmaceutical dosage form, as seen in (TABLE 5).

## CONCLUSION

The proposed methods are simple, rapid and inexpensive. So, it is good alternative to the other few reported methods and to the high cost HPLC methods.

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