MICELLAR ENHANCED SYNCHRONOUS FLUORESCENCE FOR THE ASSAY OF SUMATRIPTAN SUCCINATE IN PHARMACEUTICAL TABLETS

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ABSTRACT

Objective: To develop a sensitive, fast and selective method for the determination of sumatriptan succinate (SUM) in pharmaceutical samples.

Methods: The method is based on measuring the synchronous fluorescence of SUM using two wavelengths of (120 nm) and at a wavelength of excitation and emission of 230 nm respectively, using Agilent Technology, Cary eclipse, G9800AA model Luminescence spectrometer. The proposed method was validated in term of specificity, limit of detection, limit of quantification, precision and accuracy. The results reveal that the developed method can be applied successfully for the determination of SUM in pharmaceutical tablets.

Results: The linearity of the method was obtained with a wide range of (50-150) ng/ml with a high value of correlation coefficient value of (0.992). The limit of detection (LOD) and limit of quantification (LOQ) were found to be 1.63 and 49.5 ng/ml respectively. The accuracy of the method was found to be 99.1% with low relative standard deviation (RSD). The method was also compared statistically with the reference method using t-test and f-test, the results show no difference either in pure or pharmaceutical tablets.

Conclusion: The obtained results revealed that the developed method can be applied successfully for the determination of SUM in pharmaceutical tablets with good accuracy and precision.

Keywords: Sumatriptan, Spectrofluorimetry, Pharmaceutical preparations

INTRODUCTION

Triptans are used for the treatment of prophylaxis and acute migraine headaches in human, the most commonly used drug among triptans is sumatriptan succinate (fig. 1) it is chemically 3-[2-(diaminoethyl)]-N-methyl-indole-5-methane sulfonamide succinate. sumatriptan is a specific and selective 5-hydroxyl tryptan receptor (5HT1D) agonist with no effect on other 5HT receptors (5HT2, 5HT7) subtypes. It is officially in European Pharmacopeia [1] and United States Pharmacopeia [2].

Several methods were suggested for the determination of sumatriptan in different types of samples, including UV [3], spectrophotometric [4-6], other methods were based on high-performance liquid chromatography with various detecting systems such as UV detection [7], fluorescence detection [8] and MS detection [9, 10]. Other methods were based on and voltammetry [11]. Few methods were based on the fabrication of nanomaterial-based sensing methods [12-14]. According to the previous methods, it can be seen that most of them are based on using expensive and sophisticated techniques, this encourages us to develop a simple method for the assay of sumatriptan in the pharmaceutical samples. Spectrophotometric methods are widely used in the pharmaceutical analysis, but they have poor selectivity and sensitivity compared to spectrofluorimetry [15, 16]. The developed method is based on the enhancement of the intrinsic fluorescence of SUM, then measuring synchronous fluorescence intensity in different media. All the factors affecting the fluorescence intensities were studied, including the type of solvent, pH, temperature and micellar additives. The obtained results revealed that the developed method can be applied successfully for the determination of SUM in pharmaceutical tablets.

Fig. 1: Chemical structure of sumatriptan succinate

MATERIALS AND METHODS

Apparatus

Fluorescence intensities were measured using Agilent Technology, Cary eclipse, G9800AA model Luminescence spectrometer (Australia) equipped with a xenon arc lamp. The slit width for excitation and emission measurements were set at 5.0 nm and measured simultaneously with a constant ∆λ of 120 nm. A pH meter (HANNA model HI 2211) was used for all pH measurements.

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Materials and reagents
Reagents used were of analytical grade and deionized water was used throughout. Pure grade sumatriptan succinate were kindly supplied from Egyptian company. The pharmaceutical preparations were purchased from local drug stores oratab®100 mg tablet Tabouk company-Saudi Arabia. Sodium lauryl sulfate (SLS) 96 %, Tween 80, β-cyclodextrin, glacial Acetic acid were from BDH laboratory supplies, sodium acetate, sulphuric acid. Analytical grade solvents: acetonitrile 99.5%, methanol 99.9% dioxan 99% were obtained from Sharlau-Spain.

Standard solution
Stock solution of SUM was prepared by dissolving 0.01 g in 100 ml deionized water, then further dilutions were prepared using the given diluting solvents as appropriate and kept in the refrigerator.

General procedures

Calibration graphs
All aliquots of SUM standard solution were transferred into a series of 10-ml calibrated volumetric flasks, then 1 ml of 0.2 M acetic acid/acetate buffer of pH (5.5) was added, followed by 0.5 ml 2% SLS, mixed and then diluted to the mark using methanol as a diluting solvent to give a final concentration of (50-150 ng/ml). Then stored in the refrigerator at 10 °C for 15 min, after that the Fluorescence intensity was measured at appropriate excitation and emission wavelengths corresponding to the selected diluting solvent. The calibration curves were constructed by plotting the fluorescence intensity versus SUM concentration (ng/ml) and the regression equations were obtained.

Analysis of tablet samples
The contents of ten tablets were crushed and powdered, then a mass equivalent to 10.0 mg was weighed and transferred into a 100 ml volumetric flask, about 75 ml of methanol was added, the mixture was sonicated for 10 min, then the volume is completed to 100 ml with methanol, mixed and filtered through a 0.45 µm membrane filter. Serial dilutions covering the working concentration range of (50-150 ng/ml) were transferred into a series of 10.0 ml volumetric flasks. Then the procedure mentioned in the preparation of calibration graph was followed.

RESULTS AND DISCUSSION
Spectrofluorimetric methods of analysis are considered as sensitive and simple for the determination of many pharmaceutical active species in different samples [25, 26]. To our knowledge there is no analytical method based on native fluorescence of SUM, in this study, it was found that SUM exhibits an emission fluorescence spectrum at about 350 nm after excitation at 225 nm in aqueous medium (fig. 2)

Effect of diluting solvent
In order to study the effect of different media on the enhancement of fluorescence intensity, different organic solvents were used as diluting solvents including acetonitrile, methanol, ethanol, and dioxan. It was found that the fluorescence intensity is enhanced with the order of methanol, acetonitrile, dioxan and then ethanol as can be seen in (fig. 3). This behavior is probably due to the dynamic stabilization of the studied drug. The emission wavelengths of SUM in dioxan were 275 and 350 for acetonitrile and 294 nm for methanol. The excitation wavelength were 298, 262 nm and 253 nm of the three solvents respectively.

Fig. 2: Fluorescence spectra of SUM (100 ng/ml) in 10.0 ml of water (A) and methanol (B)

Fig. 3: Effect of diluting solvent on RFI of 10.0 ml solution of SUM (100 ng/ml), error bars represent the standard deviation of three experiments
Effect of organized media

For the better enhancement of the analytical characteristics of the fluorescence spectra of SUM, a study of the effect of different types of surfactants (cationic, anionic and nonionic) and beta-cyclodextrin was performed using the different effect of equal volume each surfactant used were summarized in (fig. 4), it can be shown that SLS gave the best enhancement of the RFI which is due to the dynamic properties of limited movement of the micellar medium of SUM [25].

Effect of pH

The effect of pH values on the fluorescence intensity was studied by using different values of pH prepared by different buffer solutions with methanol as a diluting solvent and SLS surfactant, it was found that the maximum value of fluorescence intensity was obtained at pH around 5 using acetate buffer as shown in (fig. 5), which is probably due to the formation of a non-ionizable form of the studied drug at this pH value.

In order to minimize the broadening of the emission fluorescence peaks and thus possible overlapping and minimize scattering. An alternative method for the conventional fluorescence spectrum is the use of synchronous scanning fluorescence. In this technique, the excitation and emission monochromator were scanned simultaneously and the emission intensity is recorded as a function of the excitation wavelengths. The difference between $\lambda_{em}$ and $\lambda_{ex}$ ($\Delta\lambda$) is a very important factor in the synchronous spectrum for determining the position of the bands and their intensities. In the present work the optimization of ($\Delta\lambda$) was performed by selecting different values of($\Delta\lambda$) then interpretation of the fluorescence spectrum, as a result $\Delta\lambda=120$ nm was selected because it gave sharper peak with maximum intensity, least peak overlap and increase in (RFI) as a function of concentration of SUM as shown in (fig. 6) below.

Validation of the proposed method

The developed method was validated using the following parameters: Linearity, sensitivity, LOD, LOQ, specificity, accuracy and precision.

Linearity and range

A linear relationship was established for SUM by plotting relative fluorescence intensities against different drug concentrations, the calibration curve was linear over the range 50-150 ng/ml with a high value of correlation coefficient ($r$) table 1.
Fig. 6: Calibration of SUM using the proposed synchronous method using, ($\Delta\lambda= 120$ nm) in methanol with SLS added, the concentration range is (50-150 ng/ml)

**Limit of detection (LOD) and limit of Quantitation (LOQ)**

LOD and LOQ were calculated according to ICH Q2 (R1) recommendations [ICH Expert Working Group. ICH harmonized tripartite guidelines. Validation of Analytical procedures: text and methodology [28], using the following equations and the results are shown in table 1:

$$LOD = \frac{3.3 \times S_a}{b}$$

$$LOD = \frac{10 \times S_a}{b}$$

Where $S_a$: standard deviation of the intercept and $S_b$: standard deviation of the slope of the calibration curve.

Validation of the developed spectrofluorimetric methods

**Table 1: Analytical Performance data of the proposed method**

| Parameter                        | SUM      |
|----------------------------------|----------|
| Synchronous scanning range (nm)  | 200-300  |
| $\Delta\lambda$ (nm)             | 120      |
| Linearity range (ng/ml)          | 50-150   |
| Correlation coefficient          | 0.992    |
| Slope (b)                        | 0.939    |
| Intercept (a)                    | 4.65     |
| SD of the intercept (Sa)         | 0.0021   |
| SD of the slope (Sb)             | 1.3      |
| % RSD                            | 16.3     |
| LOD* (ng/ml)                     | 49.5     |
| LOQ* (ng/ml)                     |          |

*aPercent relative standard deviation of three replicate samples, *bLimit of detection, *cLimit of quantitation

**Accuracy and precision**

To investigate the accuracy and precision of the developed method, the assay results of SUM were compared from standard reference method [28], statistical analysis of the results using student’s t-test and variance ratio F-test [30] showed no significant differences between the performance of the proposed method and reference method regarding accuracy and precision (table 2)

**Table 2: Assay results of the proposed method for SUM in pure and tablet forms compared with a reference method**

| Parameter:       | Proposed method | Reference method | % Found |
|------------------|-----------------|------------------|---------|
| Amount taken (ng/ml) | Amount found (ng/ml) | Amount taken (ng/ml) | Amount found (ng/ml) |
| 5.0              | 4.974           | 99.48            | 5.0     | 4.910           | 99.20            |
| 10.0             | 9.876           | 98.60            | 10.0    | 10.074          | 100.27           |
| 20.0             | 20.143          | 100.7            | 20.0    | 19.948          | 99.74            |
| 50.0             | 49.651          | 99.30            | 50.0    | 50.204          | 100.41           |
| *t≤SD            |                 | 99.52±0.87       |         | 99.82±0.61      |
| t-value          | 0.32            |                  |         |                  |
| F-value          | 0.57            |                  |         |                  |

Oratab® 10 mg tablet

| Amount taken (ng/ml) | Amount found (ng/ml) | Amount taken (ng/ml) | Amount found (ng/ml) |
|----------------------|----------------------|----------------------|----------------------|
| 20.0                 | 19.93                | 99.6                 | 20.0                 | 20.07                | 100.4              |
| 40.0                 | 39.76                | 99.4                 | 40.0                 | 39.89                | 99.7               |
| 60.0                 | 58.85                | 98.3                 | 60.0                 | 59.87                | 99.8               |
| *t≤SD                |                      | 99.1±0.7             |                      | 99.9±0.38             |
| t-value 0.065 (3.18) | F-value 0.450 (9.55)  |                      |                      |

*mean±SD, (SD)-standard deviation, n=3, Numbers in the parentheses are the critical tabulated values of t and F at (P=0.05)
Pharmaceutical applications

The developed method was successfully applied for the intra-day and inter-day determining (SUM) in its drug tablets on three successive days, the recovery results were obtained for the assay of SUM in pharmaceutical tablets as shown in (table 3). The results were comparable with those obtained from the reference method.

CONCLUSION

In this study, a new nonexpensive and sensitive procedure was developed for the determination of sumatriptan succinate based on the enhancement of native fluorescence of the studied drug using methanol as solvent and sodium lauryl sulfate as a micellar medium. The new method utilized the use of synchronous scanning for the determination of SUM in both pharmaceutical tablets, the method was validated and compared with reference methods.

AUTHORS CONTRIBUTIONS

All the authors have contributed equally

CONFLICTS OF INTERESTS

Declared none

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