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Determination of Zolmitriptan in Pharmaceutical Dosage Form

K. Parameswara Rao

Department of Chemistry, Andhra Loyola College, Vijayawada- 520008, India

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ABSTRACT

The spectrophotometric methods for the determination of Zolmitriptanin pure and dosage forms have been described in thispaper. The aim of the present work is to develop simple, sensitive and cost-effective spectrophotometric method for the determination of Zolmitriptan in pharmaceutical formulation. The present methods involve the determination of Zolmitriptanin pharmaceutical dosage at the given optimum conditions. The stock solution of Zolmitriptan was prepared by dissolving100 mg of the drug in 10.0 mL of methanol and made up to 100 mL with distilled water to get a clear solution. Appropriate volumes of this stock solution were diluted step wise to get the working standard solutions of concentrations 200µg/mL for Method- M_{13}; 250 µg/mL for Method-M_{15}; respectively. The proposed methods have the good sensitivity and higher λ_{max}. Statistical analysis of the results showed that the proposed procedures have good precision and accuracy.

Keywords: Zolmitriptan,Spectrophotometric Methods, Spectral Characteristics and Validation.

INTRODUCTION

Zolmitriptan(Figure 1) (S)-4-{[3-(2-dimethylaminoethyl)-1H-indol-5-yl] methyl}-1, 3-oxazolidin-2-one is an oral, selective serotonin receptor agonist used for the treatment of acute migraine attacks [1, 2].A detailed literature survey for Zolmitriptan revealed that several analytical methods such as spectrophotometric and HPLCwere reported for the quantification of Zolmitriptan that are laborious and time consuming. This made the author an attempt to assay the above said drug using simple analytical tools. This paper describes the development and validation of some new UV-Visible spectrophotometric methods and RP-HPLC for the assay of Zolmitriptan in pure and dosage forms. This paper briefs the author experimental work in developing and validating some economical analytical methods in assaying Zolmitriptan in pure and dosage forms.

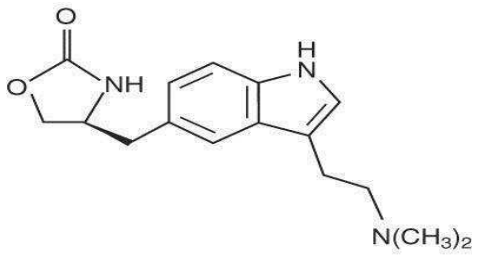


Figure 1: Molecular structure of Zolmitriptan

However, it is evident that the above said reported methods are not simple and require expensive equipment and moreover, to our knowledge no simple UV-Visible spectrometric methods have been not yet reported in the literature for the determination of Zolmitriptan in pharmaceutical dosage forms and this fact prompted the author to develop accurate and inexpensive UV-Visible spectrophotometric methods for routine determination of Zolmitriptan in pure and tablet dosage forms. Most of the reported methods require expensive instrumental setup, expertise personnel, and complicated procedure. Two of the reported visible spectrophotometric methods require liquid-liquid extraction and strict pH control. The aim of the present work is to develop simple, sensitive and cost-effective spectrophotometric method for the determination of Zolmitriptan in pharmaceutical formulation. Literature survey reveals that few analytical methods have been published for analysis of Zolmitriptan in human plasma and include high-performance liquid chromatography with coulometric [3], mass spectrometric detection [4], and liquid chromatography-mass spectrometry [5-7]. Rao et al. have presented the results on different oxide materials, polymers, nanopowders, glasses and drug materials in their earlier studies [8-60]. The present paper describes UV-Visible spectrophotometric methods**,** which are based on reactivity of the functional groups of Zolmitriptan with various organic reagents to produce colored species of reasonable stability, paving the possibility for spectrophotometric determination of Zolmitriptan in pure and pharmaceutical formulations.

MATERIALS AND METHODS

***Instruments used*:** Genesys 10 UV-Spectrophotometer 10mm matched quartzcells procured from Thermo Scientific Company with were used for all spectral measurements. A Systronics digital pH meter [Model-362] was used for pH measurements.

Preparation of Reagents:All the chemicals and reagents used were ofanalytical grade and solutions were prepared with doubled distilled water.

Method-M_{13}:Solution of TPooo solution (0.2%), HCl (0.1M) were prepared freshly with distilled water. Chloroform (Qualigens): AR grade of chloroform was used.

Method-M_{15}:Solution of WFBBL solution (0.2%), HCl (0.1M) were prepared freshly with distilled water. Chloroform (Qualigens): AR grade of chloroform was used.

Preparation of stock and working standard solutions:The stock solution (1.0 mg/mL) of Zolmitriptan was prepared by dissolving100mg of the drug in 10.0mL of methanol and made up to 100mL with distilled water to get a clear solution. Appropriate volumes of this stock solution were diluted step wise to get the working standard solutions of concentrations 200µg/mL for Method- M_{13};250µg/mL for Method-M_{15}; respectively.

Procedure for Tablets:Twenty Zolmitriptan tablets (ZOMIG; 5.0mg)were weighed, transferred to a clean dry mortar and ground into a fine powder using a pestle. Tablet powder equivalent to 100mg of drug was transferred to a 100mL volumetric flask transferred into a 100mL calibrated flask, 60mL of methanol was added and the contentshaken thoroughly for 15-20 min and the volume was finally diluted to the mark with distilled water, mixed well and filtered through Whatman filter paper No 41. A suitable volume of the filtrate was accurately diluted with distilled water and this solution was used for the determination of Zolmitriptan as per the recommended procedures described below.

RESULTS AND DISCUSSION

Method Development:It involves the Optimizationstudies for the proposedprocedures involve the study of the influence of various factors on the color development[optimal conditions] such as reagent concentration, order of addition of reagents, time, temperature and choice of solvent for maximum color development.

Recommended Procedures:After a systematic and detailed study of thevarious parameters, as described in optimum condition the following procedures (M_{13}[TPooo)] and M_{15}[WFB.BL])wereproposed for the assay of Zolmitriptan in pure and formulations.

Method-M_{13}:Into a series of 125mL separating funnels containing aliquots of standardZolmitriptan solution (0.5-2.5mL,200µg/mL), 5.0mL of 0.1M HCI solution and 2.0mL of 0.2% dye solution [TPooo] were added and the total volume of aqueous phase in each separating funnel was adjusted to 10mL with distilled water. To each separating

funnel 10mL of chloroform was added and the contents were shaken for 2min. The two phases were allowed to separate and the absorbance of the separated chloroform layer was measured atλ_{max} 480nm against a similar reagent blank. The amount of Zolmitriptan was deduced from the calibration curve (Figure 2(a&b)).

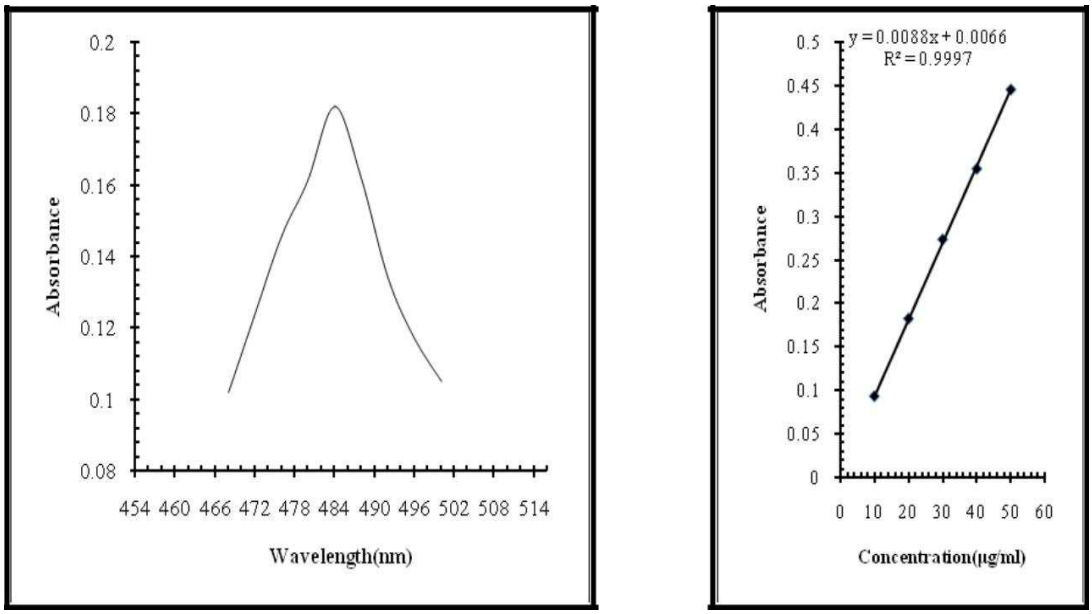


Figure 2(a&b): Absorption spectra and Beer's law plot of Zolmitriptan for Method-M_{13}

***Method-M_{15}*:**Into a series of 125mL separating funnels containing aliquots of standardZolmitriptan solution (0.5-2.5mL, 250µg/mL), 6.0mL of 0.1 M HCI solution and 2.0mL of 0.2% dye solution of WFB.BL were added successively. The total volume of aqueous phase in each separating funnel was adjusted to 10mL with distilled water. To each separating funnel 10mL of chloroform was added and the contents were shaken for 2min. The two phases were allowed to separate and the absorbance of the separated chloroform layer wasmeasured at λ_{max} 600nm against a similar reagent blank. The amount of Zolmitriptan was deduced from the calibration curve WFB.BL (Figure 3(a&b)).

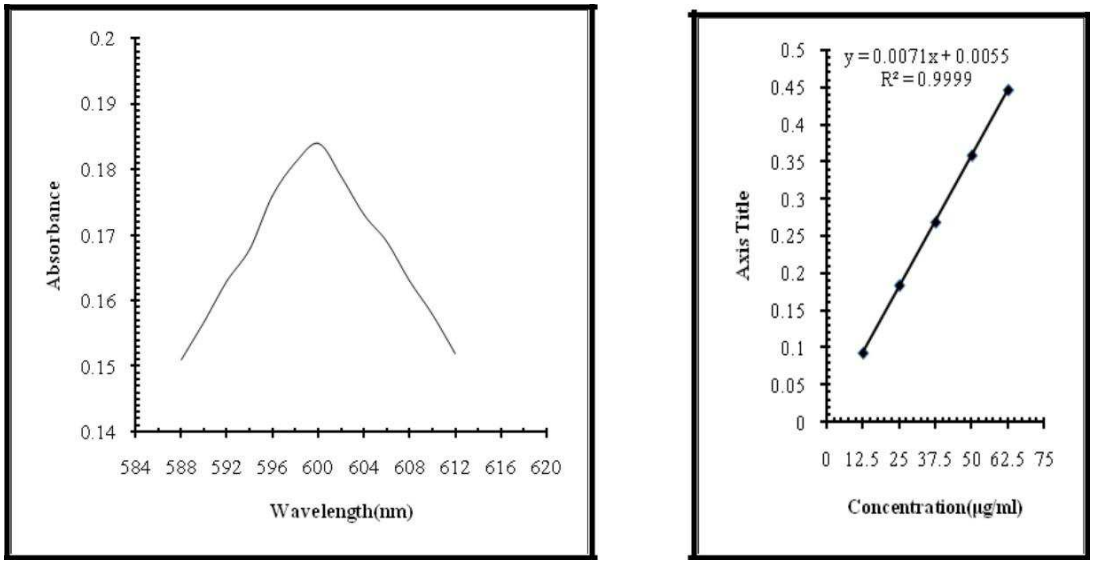
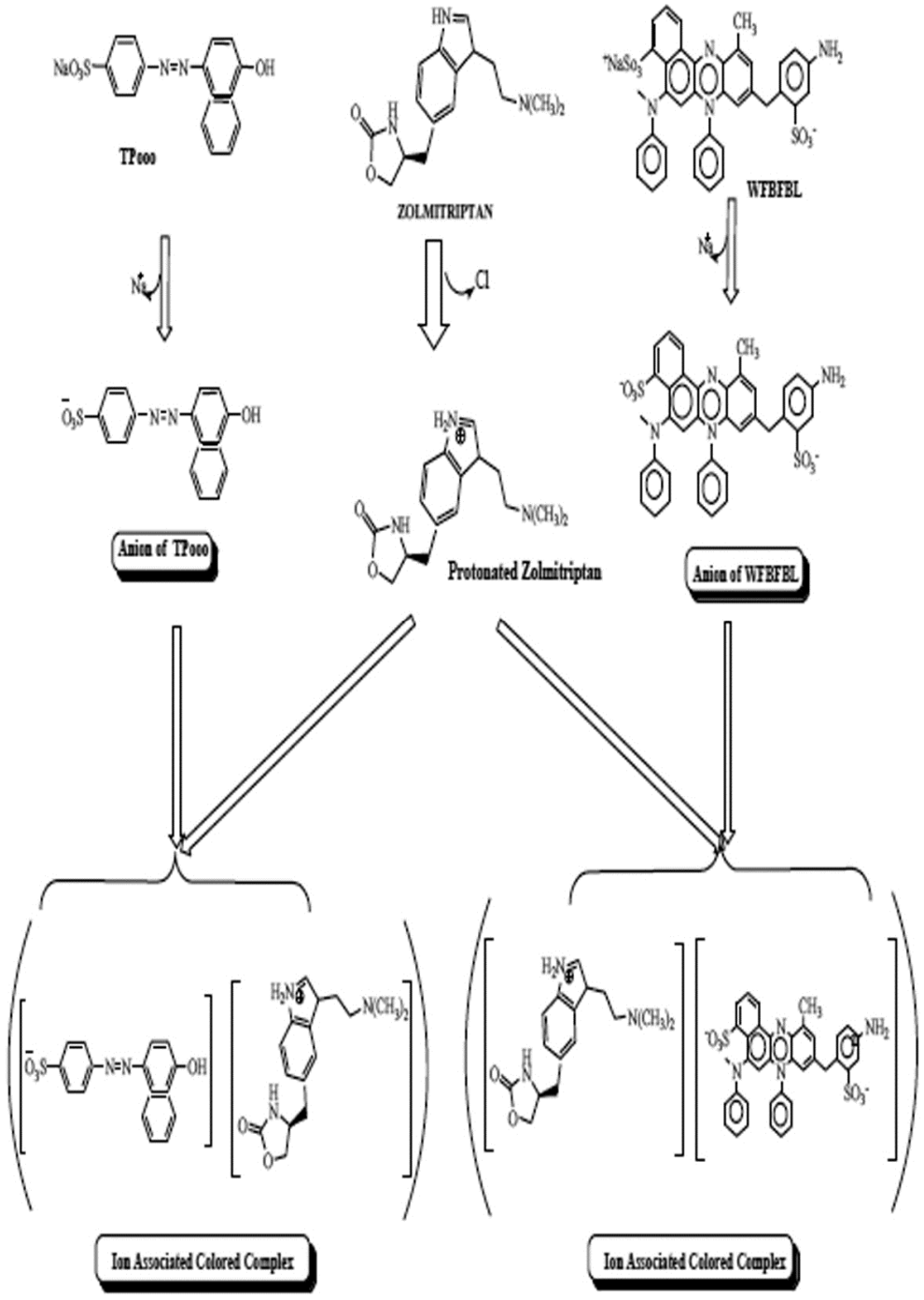


Figure 3(a&b): Absorption spectra and Beer's law plot of Zolmitriptan for Method-M_{15}



Scheme-1

Method Validation

Spectral Characteristics:The absorption spectra were scanned on aspectrophotometer in the wave length region of 340 to 900 nm against similar reagent blank or distilled water. The reagent blank absorption spectrum of each method was also recorded against distilled water. The results were graphically represented in Figure 2(a) for $M_{13}$and

Figure 3(a) for M_{15} respectively. The absorption curves of the colored species in each method show characteristic absorption maxima whereas the blank in each method has low or no absorption in this region.

Optical Characteristics:The Beer's law plots and Ringbom plots (Figure 2(b) for M_{13} and Figure 3(b) for M_{15}) of the developed methods were recorded graphically. Beer's law limits, molar absorptivity, Sandell's sensitivity and optimum photometric range for Zolmitriptan in each method were calculated. Least square regression analysis was carried out for getting the slope, intercept and the correlation coefficient values. The precision of the proposed methods was ascertained from theabsorbance values obtained by actual determination of six replicates of a fixed amount of Zolmitriptan in total solution. The percent relative standard deviation and percent range of error were calculated for the proposed methods. Recovery studies were conducted by analyzingeach pharmaceutical formulation in the instance for the active ingredient by the proposedmethods. Known amount of pure drug was added to each previously analyzed formulation and the total amount of the drug was once again determined by all proposed methods after bringing the active ingredient concentration within the Beers law limits. Commercial formulations containingZolmitriptan were successfully analyzed by the proposed methods. The values obtained by the proposed and reference method for formulations were compared statistically with F and t tests and found not to be different significantly. Percent recoveries were determined by adding standard drug to preanalyzed formulations.
Method-M_{13} & M_{15}:Zolmitriptan being a base forms an ion association complex withacidic dyes (ARS) and WFBBL which is extractable into chloroform from the aqueous phase. Based on the analogy, the structure of ion association complex is shown in Scheme-1.

CONCLUSION

The spectrophotometric methods M_{13} and M_{15} for the determination of Zolmitriptan in pure and dosage forms have been described in this paper. The present methods involve the determination of Zolmitriptan in pharmaceutical dosage at the given optimum conditions.It can be observed from the validation results of Zolmitriptan presented above, that the proposed methods have the good sensitivity and higher λ_{max}. Statistical analysis of the results showed that the proposed procedures have good precision and accuracy. Results of the analysis of pharmaceutical formulations of Zolmitriptan revealed that theproposed methods are suitable for its analysis with virtually no interference of the usual additives present in pharmaceutical formulations.

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