International Journal of ChemTech Research
CODEN( USA): IJCRGG ISSN : 0974-4290
Vol.5, No.6, pp 2941-2946, Oct-Dec 2013

# Visible Spectrophotometric Methods For The Determination Of Zolmitriptan In Bulk And Pharmaceutical Formulations Using Aromatic Aldehydes And Folin's Reagent

**P. Saifulla Khan*, P. Raveendra Reddy And V. Krishna Reddy**

**Department of Chemistry, Sri Krishnadevaraya University, Anantapuramu -515003, India.**

***Corres.author: pskhan002@gmail.com**

**Abstract**: Three simple, accurate, sensitive and extraction-free spectrophotometric methods (A, B and C) have been developed for the determination of zolmitriptan in bulk and in its pharmaceutical dosage forms. The methods A and B are based on the reaction of zolmitriptan with *p*-Dimethyl amino cinnamaldehyde (PDAC) and *p*-Dimethyl amino benzldehyde (PDAB) in the presence of sulphuricacid. The resultant red colored chromogens show maximum absorbance at 560nm and 540nm respectively. The method C is based on the formation of orange colored chromogen between zolmitiptan and 1, 2-Napthaquinone-4-sulphonic acid (NQS) in the presence of sodium hydroxide, which exhibits $\lambda_{max}$ at 485nm. Beer's law is obeyed in the concentration range 5-55µg $mL^{-1}$ for method A, 10-60 µg $mL^{-1}$ for method B and 10-80 µg $mL^{-1}$ for method C. All the methods are validated by statistical and recovery studies. The proposed methods are economical, sensitive and can be used for the determination of zolmitriptan in bulk and pharmaceutical formulations.

**Key Words:** Spectrophotometry, Zolmitriptan, p-Dimethylaminocinnamaldehyde(PDAC), p-Dimethyamino benzaldehyde(PDAB),1,2-Napthaquinone-4-sulphonicacid(NQS), sulphuric acid, sodium hydroxide, Methanol.

## Introduction:

Zolmitriptan has the chemical name (4S)-4-({3-[2-( Di methyl amino)ethyl]-1*H*-indol-5-yl} methyl)1,3-oxazolidin-2-one with molecular formula $C_{16}H_{21}N_3O_2$ and molecular weight of 287.35 g $mol^{-1}$. The basic structure of the drug is shown in fig.1. Zolmitriptan belongs to a group of medicines known as serotonin 5-HT1D receptor agonists. It works by stimulating serotonin receptor in the brain. Literature survey indicated that few analytical methods have been reported for analysis of zolmitriptan.They include some HPLC methods associated with coulometric[1], Mass spectrometric[2-4], and photometric[5-10] detectors. Other methods such as UPLC[11], voltammetric[12] and UV-Visible spectrophotometric methods[13-19] are also reported. Aromatic aldehydes (Vanillin, PDAC and PDAB etc) were employed by some researchers as chromogenic reagents for developing Spectrophotometric methods for the determination of different drugs containing amino group (both primary and secondary amines) producing Schiff's bases or enamines.[20-24] 1,2-Napthaquinone-4-sulphonic acid (NQS) was first used as a colorimetric reagent by Folin[25] for the determination of amino acids. Later on, this reagent was employed for the Spectrophotometric determination of many amino drugs.[26-31] In the present study we are reporting simple, sensitive and industry friendly spectrophotometric methods for the determination of zolmitriptan using PDAC,PDAB and NQS. The secondary amine of the cyclic imine group in the indole portion

of the drug reacts with the said reagents forming intense colored species whose absorbance was measured spectrophotometrically.

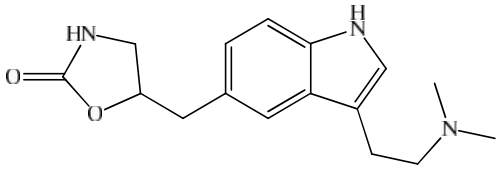


**Fig 1 Structure of Zolmitriptan**

## Materials And Methods:

**Instrument**: Shimadzu UV-1700 Pharmaspec with 1cm matched quartz cell was used for Spectrophotometric measurements.

**Reagents**: All the chemicals used were of analytical grade.

1. *p*-Dimethyl amino cinnamaldehyde (PDAC), *p*-Dimethyl amino benzldehyde (PDAB):

5% solutions of these reagents were prepared by dissolving 5gm of the aldehyde in 100mL of methanol.

2. 1,2-Napthaquinone -4- sulphonic acid (NQS) - (0.5%w/v): This solution was prepared by dissolving 500mg of reagent in 100mL Distilled water.

3. Sodium hydroxide (0.01N): 40mg of anhydrous sodium hydroxide was dissolved in 100mL distilled water.

## Experimental

A standard stock solution of the drug was prepared by dissolving 10mg of zolmitriptan in 10mL of distilled water to get a concentration of 1000 $\mu gmL^{-1}$. This was further diluted with distilled water to get the working standard solutions of 100 $\mu gmL^{-1}$.

**Assay procedure**

**Methods A and B:**

Different aliquots of standard solution of zolmitriptan (0.5-5.5mL, 100$\mu gmL^{-1}$) were transferred into series of 10mL volumetric flasks. To each flask, 1mL of *p*-Dimethyl amino cinnamaldehyde (PDAC) or *p*-Dimethyl amino benzldehyde (PDAB) (5%w/v) and 1mL of con $H_2S0_4$ were added. After thoroughly shaking, the flasks were set aside for 10 minutes for the reaction to complete. The volumes in each flask were made up to the mark with methanol. The absorbances of the red colored solutions were measured at 560 nm and 540nm against reagent blank. The colored species of PDAC and PDAB were stable for 120 and90 minutes respectively. The amount of zolmitriptan present in the sample solutions were determined from the respective calibration curves.

**Method C:**

To 1 mL of NQS (0.5%) and 1mL of 0.01N sodium hydroxide taken in each of a set of different 10mL volumetric flasks, different volumes of zolmitriptan drug solution (100$\mu gmL^{-1}$) were added. The contents were heated at $30^{o}$c for 10 minutes, allowed to stand for 10minutes and made up to the volume with distilled water. The absorbance of the resultant solution was measured at 485nm against reagent blank and plotted against the amount of the drug which gave a linear plot in the concentration range 10-80 $\mu gmL^{-1}$ of the drug.

The methods were extended for the determination of zolmitriptan in tablet formulations (zomig-2.5mg). Fifty (50) tablets were powder and an amount of the drug equal to100mg of the drug was weighed accurately and dissolved in 50mL of distilled water. The resultant mixture was sonicated for 15mins, filtered and washed with distilled water. The filtrate and the washings were combined and the final volume was made up to 100mL with distilled water. 5mL of the above solution was diluted to 50mL with distilled water to get the working

sample solution (100µgmL$^{-1}$). The solution was analyzed as described under the assay procedure for bulk samples. The analysis procedure was repeated five times to evaluate the precision.

## Results And Discussions

Both PDAC and PDAB form red colored chromogens with zolmitriptan with $\lambda_{max}$ at 560nm and $\lambda_{max}$ at 540nm respectively. They obey Beer's law in the concentration range 5-55µgmL$^{-1}$ and 10-60µgmL$^{-1}$ respectively. The color complexes formed between Zolmitriptan and PDAC as well as PDAB are shown in figures 2 and 3 respectively (Methods A and B).

The method C is based on 1,2-Napthaquinone -4-sulphonic acid forming orange colored complex with zolmitriptan in alkaline conditions. The drug zolmitriptan derevatizes with NQS forming orange colored chromogen with $\lambda_{max}$ at 485nm obeying Beer's law in the concentration range 10-80µgmL$^{-1}$.The proposed reaction is shown in figure 4.

In all the three methods systematic and detailed study on the various parameters such as reaction time, effect of reagent concentration and solvents effects on reaction were carried out and the optimum conditions were established. The optical characteristics such as absorption maximma, Beer's law limits, molar absorptivity, Sandell's sensitivity and the regression analysis using the method of leastsqure and the correlation coefficient of the regression plots were evaluated and summarized in Table-1. The reproducibility and precision of the methods are very good as shown by the corresponding RSD values. To assess the applicability of the proposed methods, they were employed for the determination of zolmitriptan in zomig2.5mg commercially available tablets from local pharmacy. The results obtained in the studies are presented in the Table-2. The recovery percentage of the drug was evaluated by spiking different known amounts of zolmitriptan in to the drug sample and determining their amounts by the proposed methods. In all the methods 99.0 to 100.0% recoveries were achieved which indicates the selectivity of the proposed methods.

**Table 1 Optical Characteristics And Precision Data**

| Parameters | Method A | Method B | Method C |
|---|---|---|---|
| $\lambda_{max}$ (nm) | 560 | 540 | 485 |
| Beer's law limits(µgmL$^{-1}$) | 5-55 | 10-60 | 10-80 |
| Molar Absorptivity(Lt mole$^{-1}$cm$^{-1}$) | 4.668x10$^3$ | 4.237x10$^3$ | 3.103x10$^3$ |
| Sandell's Sensitivity (µg cm$^{-2}$ /0.001 absorbance unit) | 0.0615 | 0.0677 | 0.0925 |
| Regression Equation* (Y= mx +c)<br>Slope(m)<br>Intercept(c) | <br><br>0.017<br>-0.006 | <br><br>0.015<br>-0.017 | <br><br>0.011<br>-0.015 |
| Correlation Coefficient (r) | 0.999 | 0.999 | 0.999 |
| Precision(% RSD) | 0.295 | 0.380 | 0.455 |

**Table 2 Assay of Zolmitriptan in Zomig Tablet Formulations**

| S.No | Labeled Amount( mg) | *Amount obtained by proposed method (mg) | | | ** % Recovery by the proposed method | | |
|---|---|---|---|---|---|---|---|
| | | Method A | Method B | Method C | Method A | Method B | Method C |
| 1 | 2.5 | 2.49 | 2.47 | 2.46 | 100.15 | 99.55 | 99.95 |
| 2 | 2.5 | 2.46 | 2.49 | 2.45 | 100.00 | 99.85 | 99.79 |
| 3 | 2.5 | 2.48 | 2.45 | 2.42 | 99.89 | 100.25 | 98.50 |

* Average five determinations. ** After spiking the sample.

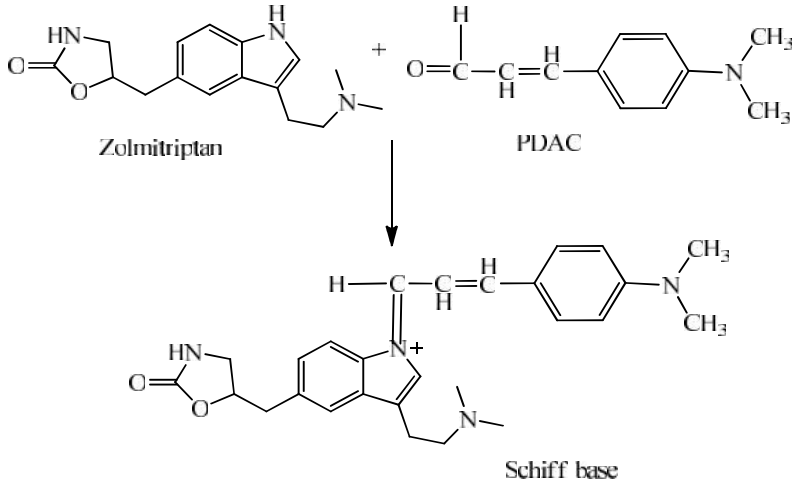


**Fig 2 Proposed reaction mechanism between Zolmitriptan and PDAC.**

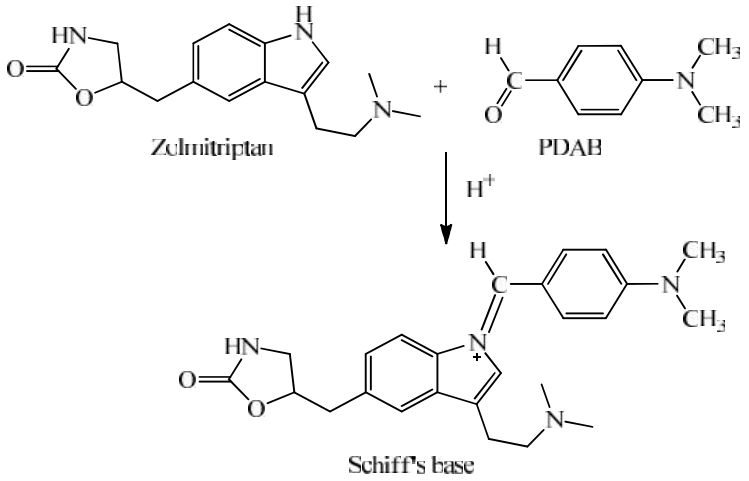


**Fig 3 The reaction mechanism between Zolmitriptan and PDAB.**

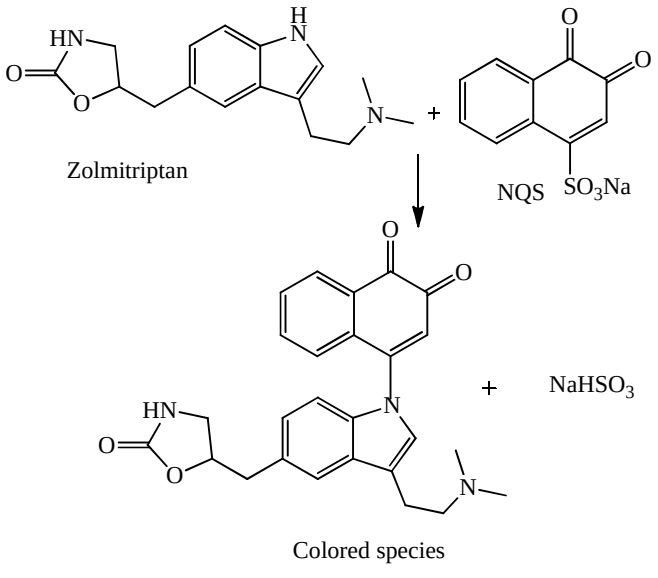


**Fig 4 Proposed reaction between Zolmitriptan and NQS.**

## Conclusion:

The proposed methods are simple, extraction-free, sensitive, accurate and economical for routine analysis of zolmitriptan in bulk and its pharmaceutical formulation. Based on molar absorptivity data and Beer's law range, it may be concluded that among the proposed methods, method A is more sensitive than method B which in turn is more sensitive than the method C.

## Acknowledgement

The authors acknowledge M/s Vishnu Chemicals Limited, Hyderabad for the supply of Zolmitriptan as gift sample.

## References

1. Clement, EM and Franklin, M. Simultaneous measurement of zolmitriptan and its major metabolites *N*-desmethylzolmitriptanand zolmitriptan *N*-oxide in human plasma by High-Performance Liquid chromatography with coulometric detection. Journal of Chromatography B.2002; 766 (2): 339–343.
2. Yao, J, Qu, Y, Zhao, X. et al. Determination of zolmitriptan inhuman plasma by high performance liquid chromatography electro spray mass spectrometry and study on its pharmacokinetics. Journal of Chinese Pharmaceutical Sciences.2005; 14 (1):25-28.
3. Zhang, Z, Xu, F, Tian, Y, Li, W and Mao, G. Quantification of zolmitriptan in plasma by high-performance liquid chromatography-electro spray ionization mass spectrometry.Journal of Chromatography B.2004; 813 (1-2): 227–233.
4. Wang, D, Ouyang, DS, Tan, ZR. et al. HPLC-MS determination of zolmitriptan in human plasma and research of its bioequivalence. Chinese Journal of Pharmaceutical Analysis. 2007; 27(2): 171–173.
5. Vijayakumar, EKS, Samel, MA, Bhalekar,SB and Pakhale,SM. A new stability indicating HPLC method for related substances in zolmitriptan. Indian Journal of Pharmaceutical Sciences. 2010; 72(1):119–122.
6. Annapurna, MM and Nanda, B. Validated RP method for the determination of zolmitriptan-a serotonin 5-HT receptor agonist. Journal of Pharmacy and Nutrition Sciences. 2011; 1(1): 9–14.
7. Sankar, DG, Nagesh Babu, A, Rajeshwari, A and Vamsi Krishana, M. Development and validation of RP-HPLC method for estimation of zolmitriptan in tablet dosage forms. Asian Journal of Chemistry. 2009; 21(7): 5019–5022.
8. Srinivasu, MK, Rao, BM, Sridhar, G, Kumar, PR, Chandrasekhar, KB and Islam, A. A validated chiral LC method for the determination of Zolmitriptan and its potential impurities. Journal of Pharmaceutical and Biomedical Analysis. 2005; 37(3): 453–460.
9. Sagar, PV, Kumar, D, Dey, S and Samal, HB. Simultaneous estimation of rizatriptan, sumatriptan and zolmitriptan by RP-HPLC method in bulk. Journal of Pharmacy Research.2010; 3 (12): 2930–2933.
10. Induri, M, Bhagavan, RM, Rajendra, PY, Pavankumar, RK, Boddu, R and Sarva, R. A validated RP-HPLC method for the quantification of zolmitriptan in tablet dosage form. Der Pharma Chemica.2010; 2(5): 351–357.
11. Reddy, YK, Reddy, GVS, and Jayaveera, KN. A new stability indicating RP-UPLC method for related substances in zolmitriptan. African Journal of Scientific Research. 2011; 1(1): 50–62.
12. Uslu, B and Canbaz, D. Anodic voltammetry of zolmitriptanat boron-doped diamond electrode and its analytical applications. Pharmazie. 2010; 65(4):245–250.
13. Acharjya, SK, Rao, MEB, Kumar, BVVR and Annapurna, MM. UV-Spectrophotometric methods for the determination of zolmitriptan in bulk and pharmaceutical dosage Forms. Journal of Advanced Scientific Research. 2011; 2(3): 42–47.
14. Murthy, TEGK and Veditha, K. Spectrophotometric estimation of zolmitriptan. Indian Pharmacist.2011; 9(12): 57–60.

15. Sankar, DG, Babu, AN, Rajeswari,A, Krishna, MV and Devi, KN. Spectrophotometric determination of zolmitriptan in pharmaceutical dosage forms. Asian Journal of Chemistry.2008; 20(6): 4960–4962.
16. Raza, A, Ansari, TM, and Niazi, SB. A novel Spectrophotometric method for the determination of zolmitriptan in pharmaceutical formulations. Journal of the Chinese Chemical Society. 2007; 54(6): 1413–1417.
17. Aydogmus, Z and Inanli,I. Extractive Spectrophotometric methods for determination of zolmitriptan in tablets. Journal of AOAC International. 2007; 90(5) 1237–1241.
18. Gouda, AA, Sheikh, RE, and El-Azzazy, RM. Charge transfer Spectrophotometric determination of zolmitriptan in pure and dosage forms. Journal of analytical bioanalytical techniques.2012; 3(6): 1000149.
19. Prashanth, KN, Basavaiah, K and Raghu, MS. Spectrophotometric determination of zolmitriptan in bulk drug and pharmaceuticals using vanillin as a reagent. ISRN Analytical chemistry.2013; Article ID 790382, 7.
20. Narayana, B, Krishnamurthy, A, Narayana shetty, D and Veena, K. Spectrophotometric Determination of Ranitidine Hydrochloride Based on the Reaction with p-Di methylamino benzaldehyde. Eurasian journal of analytical chemistry. 2010; 5(1):63-72.
21. Siddappa, K, Mallikarjuna, M, Reddy, PT and Tambe, M. Spectrophotometric determination of Metronidazole through Schiff's base system using Vanillin and PDAB reagents in pharmaceutical preparations. Ecletica Quimica.2008; 33(4): 41-46.
22. Gowri sankar, D, Sastry, CSP, and Narayanareddy, M. The Determination of resorcinol amines with aromatic aldehydes. Indian drugs.1991; 28(6):269-273.
23. Joseph, BL and Wallace, RB. Condensation of secondary amines with aldehydes and naphthols. Journal of American chemical society.1930; 52(4): 1655-1659.
24. Youngman, MA, and Dax, SL. Solidphase Mannich condensation of amines, aldehydes and alkynes: investigation of diverse aldehyde inputs. Journal of combinatorial chemistry. 2001; 3(5): 469-472.
25. Folin, O. A system of blood analysis: supplement III. A new colorimetric method for determination of the amino-acid nitrogen in blood. Journal of Biological chemistry.1922; 51: 377-391.
26. Kumar, CHA, Kumar, TA, Gurupadayya, BM, Sloka, SN, Reddy, BMR. Novel spectrophotometric determination of valacyclovir and cefotaxime using 1, 2-napthaquinone-4-sulfonic acid sodium in bulk and pharmaceutical dosage form. Archives of Applied Science Research.2010; 2 (4): 278-287.
27. Mahmoud, AM, Khalil, NY, Darwish, IA, Aboul-Fadl, Y. Selective spectrophotometric and spectrofluorometric methods for the determination of amantadine hydrochloride in capsules and plasma via derivatization with 1,2-naphthoquinone-4-sulphonate. International journal of analytical Chemistry.2009; 2009(810104).
28. Al-Momani, IF. Spectrophotometric determination of selected cephalosporin's in drug formulations using flow injection analysis. J Pharm Biomed Anal 2001, 25(5-6): 751-757.
29. Darwish, IA. Kinetic Spectrophotometric methods for determination of trimetazidine di hydrochloride. Analytica Chimica Acta. 2005; 551(1-2): 222-231.
30. Darwish, IA, Abdine, HH, Amer, SM, Al-Rayes, LI. Simple Spectrophotometric method for the determination of paroxetine in tablets using 1,2-naphthoquinone-4-sulphonate as a chromogenic reagent. International journal of analytical Chemistry.2009, 2009(237601) .
31. Darwish, IA, Abdine, HH, Amer, SM, Al-Rayes, LI. Spectrophotometric Study for the Reaction of Fluvoxamine 1,2-naphthoquinone-4-sulphonate :Kinetic, Mechanism, and Use for Determination of Fluvoxamine in its Dosage Forms. Spectrochimica Acta A. 2009;72(4):897-902.

★★★★★