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Research Article

ION ASSOCIATION METHOD FOR THE DETERMINATION OF SUMATRIPTAN SUCCINATE FROM TABLET DOSAGE FORMS USING TROPAEOLIN OOO

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ABSTRACT

A simple, sensitive, rapid and accurate extractive spectrophotometric method has been developed for the determination of sumatriptan succinate from bulk and tablet dosage forms. The method is based on the formation of orange red colored chloroform extractable ion-pair complex between the basic nitrogen of the drug and acidic dye Tropaelin ooo (TPOOO) in the presence of 0.1M HCl with an absorption maximum of 482.5 nm. The calibration graph is linear over the concentration range of 2-10µg/ml and its Molar absorptivity and Sandell's sensitivity are $2.0830x10^4$ l/mol/cm and 0.019851 µg/cm^2/0.001 absorbance units respectively. The proposed method is applied to commercial available tablets and the results are statistically compared with those obtained by the UV reference method and validated through recovery studies.

Keywords: Beer's Law, Chloroform, Extraction, Spectrophotometry, Sumatriptan, Tropaeolin OOO.

INTRODUCTION

The Sumatriptan succinate (SUM) (Fig.1) is the most frequently prescribed anti- migraine drug of triptan class. It is chemically known as 3-[2-(Dimethylamino) ethyl] –N-methyl-1H indole -5-methane sulphonamide succinate (1:1) base [1].

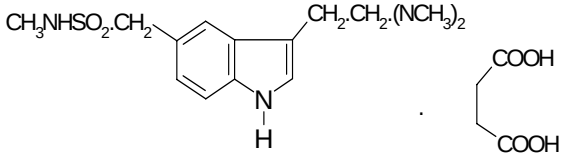

Fig. 1: Chemical structure of SUM

SUM is a specific and selective 5- hydroxyl tryptamine receptor (5-HT_{1D}) agonist with no effect on the other 5HT receptor ($5HT_2$-5 HT_7) sub types. It is used widely for prophylaxis and acute relief of migraine attack with or without aura. SUM undergoes an extensive biotransformation mainly through Mono amino oxidase-A. The drug is official in EP [2] and USP [3] suggests chromatographic methods for determination of SUM in bulk and tablet formulations. Several analytical techniques like HPLC [4-9], HPLC-MS-MS [10-13], HPLC- ECD [14-15], HPLC-coulometry [16], capillary LC-MS-MS [17], HPTLC [18], spectrophotometric with HPTLC [19], RP-HPLC and colorimetric[20], UV[21], voltametry[22], capillary electrophoresis[23], and densitometry with spectrophotometric detection[24] have been reported in the literature. The main purpose of the present study was to establish a relatively simple, sensitive, validated and inexpensive visible spectrophotometric method for the determination of SUM in pure form and in pharmaceutical dosage forms, since most of the previous methods involve sophisticated equipments which are costly and pose problems of maintenance. So the authors have made some attempts in this direction and succeeded in developing a method based on the reaction between the drug and acidic dye Tropaeolin ooo in the presence of 0.1M HCl. The method can be extended for the routine quality control analysis of pharmaceutical products containing SUM.

As the extraction spectrophotometric procedures are popular for their sensitivity and selectivity in the assay of drugs, the acid dye technique [25] was therefore, utilized in the present work for the estimation of SUM. The present paper describes simple and sensitive extraction spectrophotometric method for the determination of SUM, based on its tendency to form chloroform extractable ion-association complex with acidic dye belonging to Azo (monoazo) category dye TP000 (CI No. 15510) under experimental conditions by exploiting the basic nature of the drug molecule.

MATERIALS AND METHODS

A Systronics UV/Visible spectrophotometer model -2203 with10mm matched quartz cells was used for all spectral measurements. A pure drug sample of SUM was provided as a gift sample by Orchid health care Ltd., India. All the chemicals used were of analytical grade. Tropaeolin 000 (Fluka, 0.2%, $5.7x10^{-3}$M prepared by dissolving 200mg of Tropaeolin 000 in 100ml distilled water and subsequently washed with chloroform to remove chloroform soluble impurities), 0.1M HCl (prepared by diluting 8.7ml of Con. Hydrochloric acid to 1000ml with distilled water and standardized) were prepared.

Standard solution: The standard stock solution (1mg/ml) of SUM was prepared by dissolving 100mg of SUM initially in 10ml of 0.1M sodium hydroxide and followed by dilution to 100 ml with distilled water. The working standard solution of SUM (100µg/ml) was obtained by appropriately diluting the standard stock solution with the same solvent.

Sample solution: About 20 tablets were pulverized and the powder equivalent to 100mg of SUM was weighed, dispersed in 25ml of IPA, sonicated for 30 minutes and filtered through Whatman filter paper No 41.The filtrate was evaporated to dryness and the residue was dissolved as under standard solution preparation.

Assay: Aliquots of the standard SUM solution (0.5ml-2.5ml, 100µg/ml) were placed in a series of 125ml separating funnels. A volume of 6.0ml of 0.1M HCl and 2.0ml of TPOOO were added. The total volume of aqueous phase in each separating funnel was adjusted to 15.0ml with distilled water. Then 10.0ml of chloroform was added to each funnel and the contents were shaken for 2 minutes. The two phases were allowed to separate and the absorbance of the separated chloroform layer was measured at 482.5nm (Fig. 2 showing absorption spectra) against a reagent blank within the stability period (5minutes to 1hour). The amount of drug was computed from its calibration graph (Fig.3 showing Beer's Law plot).

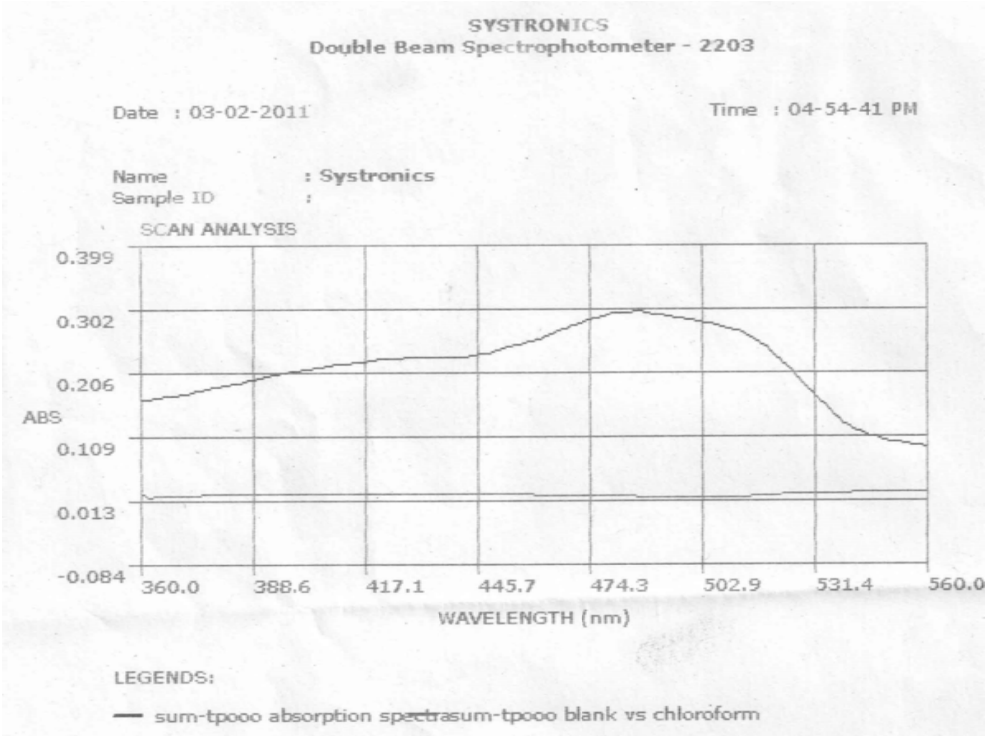

Fig. 2: Absorption spectra of SUM-TPOOO

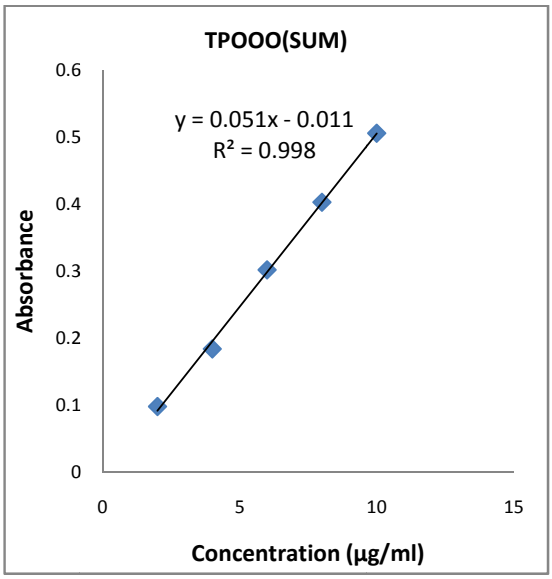

Fig. 3: Calibration graph of SUM-TPOOO

RESULTS AND DISCUSSION

Optimum operating conditions used in the procedure were established by adopting variation of one variable at a time (OVAT) method. The effect of various parameters such as time, volume and strength of TPOOO reagent and acid solution and solvent for final dilution of the colored species were studied. The water immiscible solvents tested for the extraction of colored complex into organic phase include chlorobenzene, dichloromethane, carbon tetra chloride, benzene, n-butanol or chloroform. Chloroform was preferred for its selective extraction of colored drug -dye complex into organic layer from the aqueous phase. The stoichiometric ratio of the drug to dye was determined by the slope ratio method and was found to be 1:1. The optical characteristics such as Beer's law limit, Sandell's sensitivity, molar absorptivity, percent relative standard deviation (calculated from the six measurements containing $3/4^{th}$ of the amount of the upper Beer's law limits), Regression characteristics like standard deviation of slope (Sb), standard deviation of intercept (Sa), standard error of estimation (Se) and % range of error (0.05 and 0.01 confidence limits) were calculated and the results are summarized in Table-1.

Table 1: Optical and regression characteristics, precision and accuracy of the proposed method.

Parameter	Values
λ_{max} (nm)	482.5nm
Beer's law limit(µg/ml)	2 - 10
Sandell's sensitivity (µg/cm²/0.001 abs. unit	0.019851117
Molar absorptivity (Litre/mole/cm)	20830.0625
Correlation Coefficient	0.998
Regression equation (Y)*	
Intercept (a)	-0.011
Slope(b)	0.051
%RSD	0.9524
% Range of errors(95% Confidence limits)	
0.05 significance level	0.9996
0.01 significance level	1.5677

*Y = a+bx, where Y is the absorbance and x is the concentration of sumatriptan in µg/ml

Commercial formulations containing SUM were successfully analyzed by the proposed method. The values obtained by the proposed and reference methods for formulations were compared statistically by the t-and f-test and found not to differ significantly.

As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the preanalyzed formulations at three different concentration levels (50%, 75% and 100%). These results are summarized in Table-2.

Table 2: Results of analysis of tablet formulations containing SUM

Method	*Formulations	Labeled amount (mg)	Found by proposed methods			Found by reference method ± SD	#% Recovery by proposed method ± SD
			**Amount found ± SD	t	f		
SUM-TPOOO	Tablet-1	50	49.654 ± 0.1568	0.108	1.580	49.647 ±0.125	99.307 ± 0.314
	Tablet-2	50	49.709 ± 0.190	0.1696	1.277	49.702 ± 0.169	99.418± 0.381

* Different batches (Tablet1 &2) from two different companies (Sun Pharmaceuticals, Dabur Pharmaceuticals)
**Average ± Standard deviation of six determinations, the t- and f-values refer to comparison of the proposed method with reference method. (UV). Theoretical values at 95% confidence limits t =2.57 and f = 5.05.
Recovery of 10mg added to the pre analyzed sample (average of three determinations).
Reference method (reported UV method) using double distilled water (λ_{max}=220nm).

CONCLUSION

The reagents utilized in the proposed method are normal cost, readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The proposed extractive colorimetric method is validated as per ICH guide lines and possess reasonable precision, accuracy, simple, sensitive and can be used as alternative method to the reported ones for the routine determination of SUM depending on the need and situation.

Chemistry of colored species

The positively charged tertiary nitrogen of SUM molecule in acid medium is expected to attract the negatively charged part of the acidic dye TPOOO and form an ion pair held together through electrostatic attraction. Based on the analogy, the structure of ion association complex in this method is shown in the scheme (Fig.4).

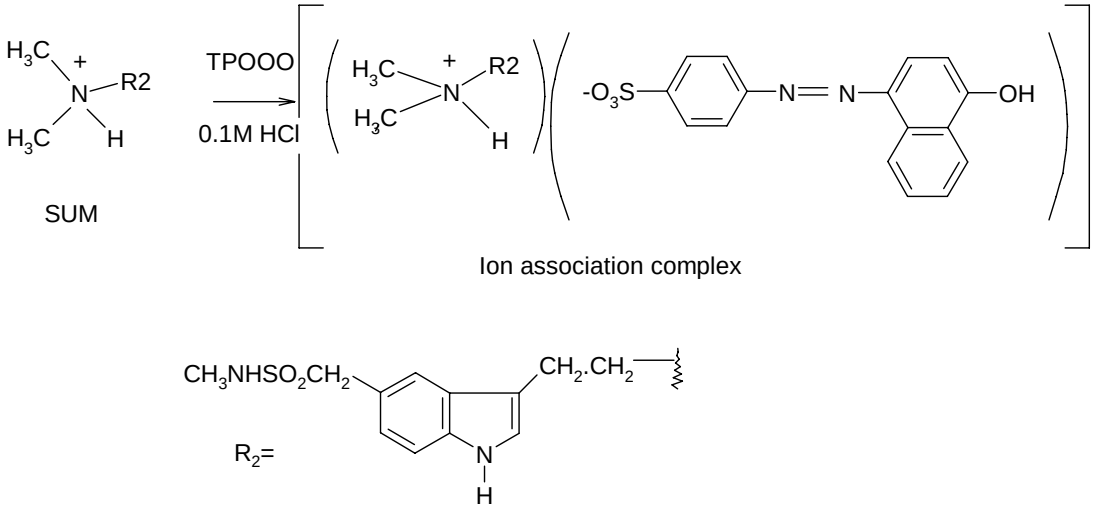

Fig. 4: Scheme of the reaction

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REFERENCES

1. J.E.F. Reynolds In. Martindale the Extrapharmacopia, 30thed.The Pharmaceutical Press, London, 1993: 417.
2. EP, European Pharmacopoeia, 6th edition, 2008; vol.2: 3005.
3. USP, The United States Pharmacopoeia, 31st Revision, US Pharmacopoeial Convention Inc. Rockville, MD, 2008; vol.3: 3310.
4. Ge Z, Tessier E, Neirinck L and Zhu Z. HPLC method for the determination of sumatriptan with fluorescence detection in human plasma. J Chromatogr B Analyt Technol Biomed Life Sciences 2004; 806: 299-303.
5. Majithiya R.J, Majithiya J.B, Umrethia M.I and Murthy Y. HPLC method for the determination of sumatriptan in plasma and brain tissue. Ars Pharmaceutica 2006; 47: 199-210.
6. Ravi S, Dawis Y and Khan N. Development and validation of an RP-HPLC-UV method for analysis of sumatriptan in dosage forms. Acta chromatographica 2009; 21 (3): 421-432.
7. Shirisat V.A, Gabhe S.Y and Deshpande S.G. HPLC Determination of Sumatriptan from pharmaceutical preparations. Indian drugs1998; 35 (7): 404-407.
8. Sukhadev Singh and Jain R. HPLC method for the determination of sumatriptan. Indian Drugs1997; 34(9): 527-531.
9. Badwe N, Sharma N, Agarwal N. HPLC method for the determination of sumatriptan. Eastern Pharmacist1997; XL (475): 121-122.
10. Boulton D.W, Duncan G.F and Vachharajani N.N. Validation and application of HPLC/ tandem mass spectrometry assay for sumatriptan in human plasma. Biomed. Chromatography B 2003; 17(1): 48-52.
11. McLoughlin D.A, Olah T.V, Ellis J.D and Gilbert J.D. Quantization of the $5HT_1D$ agonist and sumatriptan in plasma by LC atmos. pressure chemical ionization mass spectrometry. J Chromatograph A 1996; 726: 115-124.
12. Cheng K.N, Redrup M.J, Barrow A and Williams P.N. Validation of LC tandem mass spectrophotometric method for determination of Sumatriptan in human biological fluids. J Pharm. Biomed Anal 1998; 17(3): 399-408.
13. Oxford J and Lant M. LC-MS method for the determination of sumatriptan. J Chromatograph 1989; 496(1): 137-140.
14. Dunne M and Andrew P. Fully automated assay for the determination of Sumatriptan in human serum using solid phase extraction and HPLC with electrochemical detection. J Pharm. Biomedical Anal 1996; 14: 721-726.
15. Andrew P.D, Birch H.L and Phillpot D.A. The determination of sumatriptan in plasma and urine by HPLC with electrochemical detection. J Pharm. Sci. 1993; 82: 73-76.
16. Franklin M, Odontiadis J and Clement E.M. The determination of Sumatriptan in human plasma by HPLC with coulometric detection and utilization of solid phase extraction. J Chromatography B Biomed Sci. Appl. 1996; 681: 416-420.
17. Moneti G. Analysis of sumatriptan in cerebro Spinal fluid using capillary LC/MS/MS. In; from: http:/wwwl.dionex.com/enus/literature/lp56178.html.
18. Shah C.R, Suhagia B.N, Shah N.J and Shah R.R. Development and validation of a HPTLC method for estimation of sumatriptan in dosage forms. Indian J Pharm. Sci.2008; 70(6): 831-834.
19. Tipre D.N and vavia P.R. Estimation of sumatriptan by spectrometric and HPTLC method. Indian Drugs 1999; 36(8): 501-505.
20. Avadhanulu A.B, SrinivasJ.S and Anjaneyulu Y. RP-HPLC and Colorimetric method for the determination of sumatriptan in its drug form. Indian Drugs1996; 33(7): 334-337.
21. Prabakar A.E, Kalaichelvi R, Thangabalan B , Karthikeyan R, Ch. Prabakar and Vijay kumar. Validated spectroscopic method for estimation of sumatriptan succinate in pure and from tablet formulations. Research J Pharm. and Tech 2009; 2(3): 495.
22. Sagar K, Alvarez J.M.F, Hua C, Smyth S.R and Munden R. The determination of sumatriptan by Voltametry. J Pharm. Biomed Anal 1992; 10(1): 17-21.
23. Altria K.D and Filbey S.D. Determination of sumatriptan by capillary electrophoresis. Anal Proc 1993; 30: 363.
24. Bebawy L.I, Moustafa A.A and Abo-Talib N.F. Densitometry and spectrophotometric detection of sumatriptan. J Pharm. Biomed Anal 2003; 32: 1123.
25. Beckett A.H. and Stenlake J.B, Practical Pharmaceutical chemistry, Vol. II, IV edition, CBS Publishers, New Delhi, 1997: 304.
26. ICH, Q2(R1), Harmonized Tripartite Guideline, Validation of Analytical procedures Text and methodology, International conference on Harmonization(ICH), Geneva, Nov. 2005.