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A SIMPLE COLORIMETRIC DETERMINATION OF SUMATRIPTAN SUCCINATE FROM TABLET DOSAGE FORMS USING COBALT THIO CYANATE

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1. ABSTRACT

A simple, sensitive and cost effective visible 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 green colored coordination complex by the drug with cobalt thiocyanate which is quantitatively extractable into nitro benzene with an absorption maximum of 629.4 nm. The calibration graph is linear over the concentration range of 16-48µg/ml with a Molar absorptivity of $3.9696X10^3$ l/mol/cm. The proposed method is applied to commercial available tablets and the results are statistically compared with those obtained by the reference method and validated by recovery studies.

2. KEY WORDS: Sumatriptan, Cobalt thiocyanate, Nitro benzene, Extractive Spectrophotometry.

3.INTRODUCTION

The Sumatriptan succinate (SUM) (figure-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]. SUM is a specific and selective 5- hydroxyl tryptamine receptor ($5\text{-}HT_{1D}$) 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] and 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 with colorimetric [20], UV [21] and voltametry [22], capillary electrophoresis[23],densitometry and 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 maintance. So the authors have made some attempts in this direction and succeeded in developing a method based on the reaction between the drug and cobalt thiocyanate [25]. The method can be extended for the routine assay of SUM formulations.

4. MATERIALS & METHODS (EXPERIMENTAL)

A Systronics UV/Visible spectrophotometer model -2203 with10mm matched quartz cells was used for all spectral measurements. A Systronics µ- pH meter model-362 was used for pH measurements. All the chemicals used were of analytical grade.CTC ($2.50x10^{-1}$M, solution prepared by dissolving 7.25 g of cobalt nitrate and 3.8 g of ammonium thiocyanate in 100ml distilled water), Citrate buffer pH(2.0) (prepared by mixing 306ml of .01M trisodium citrate with 694ml of 0.1M HCl and pH was adjusted to 2.0) were prepared.

Standard and sample drug solution: An accurately weighted quantity of SUM (pure or tablet powder) equivalent to 100mg was dissolved in 100ml of distilled water to get 1mg/ml stock solution. From this, 40ml stock solution was mixed with 5ml of 1M Na_2CO_3 solution and transferred into 125ml separating funnel. The freebase released was extracted with 3x15ml portions of chloroform. The total chloroform extract was evaporated to dryness and made up to 100ml with distilled water to obtain 400µg/ml working standard solution.

Assay: Aliquots of standard SUM solution (1.0ml-3.0ml, 400µg/ml) were delivered into a series of 125ml separating funnels. Then 2.0ml of buffer solution (pH2.0) and 5.0ml CTC solution were added. The total volume of aqueous phase in each separating funnel was adjusted to 15.0ml with distilled water. To each separating funnel 10.0ml of

nitrobenzene was added and contents were shaken for 2 minutes. The two phases were allowed to separate and absorbance of nitrobenzene layer was measured at 629.4nm against a similar reagent blank (Fig-2 showing absorption spectra, Fig-3 showing Beer's law plot).The colored product was stable for 1 hour. The amount of SUM in the sample solution was computed from its calibration graph.

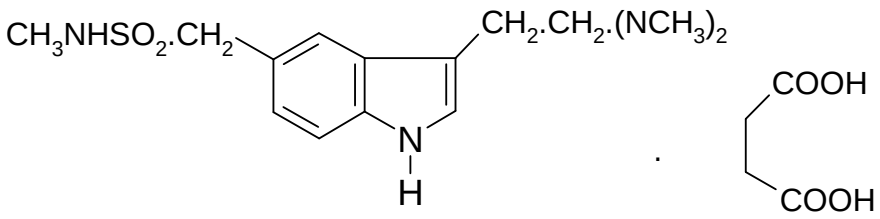

Figure- 1 Showing Chemical Structure of SUM

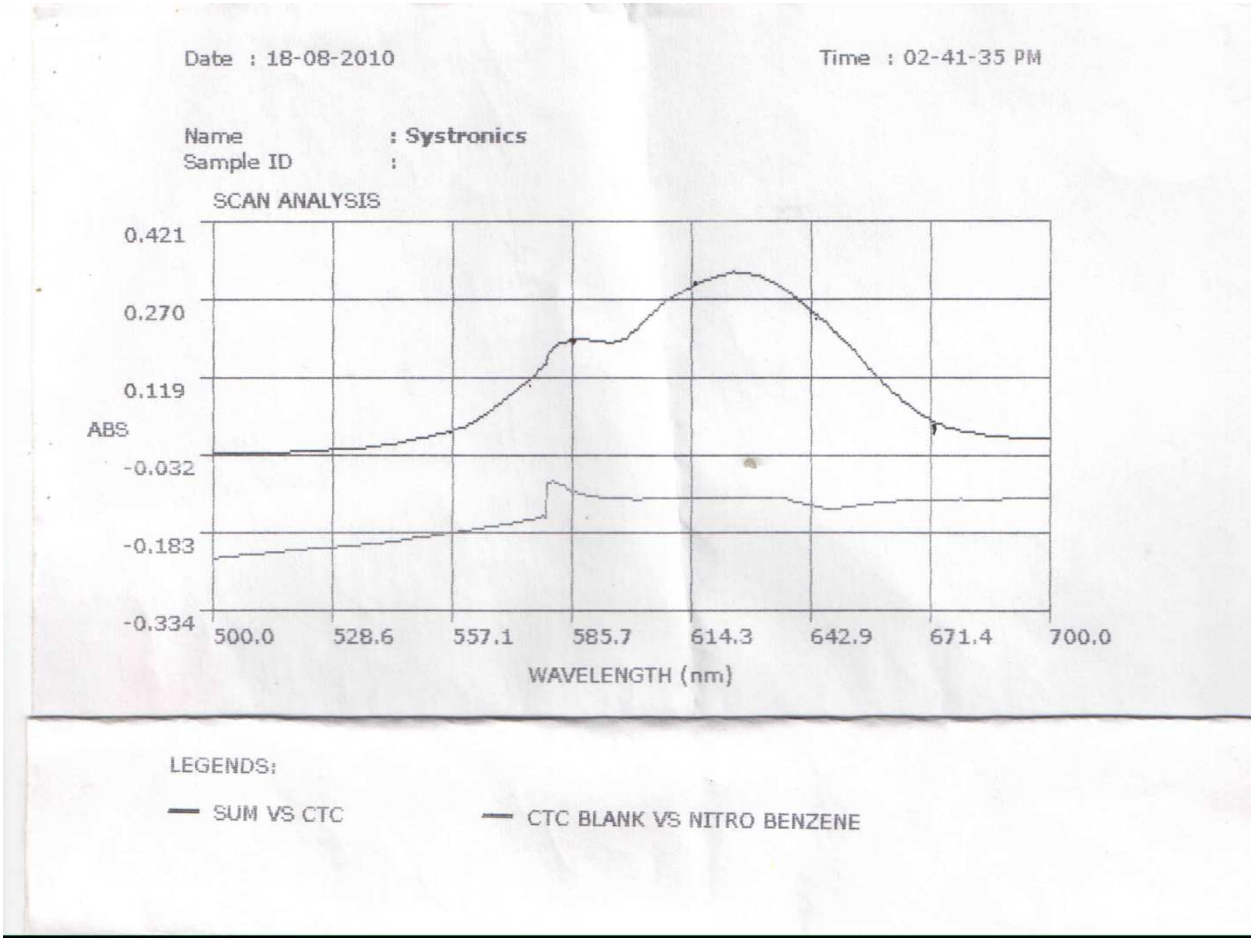

Figure 2 Showing Absorption Spectra of SUM-CTC

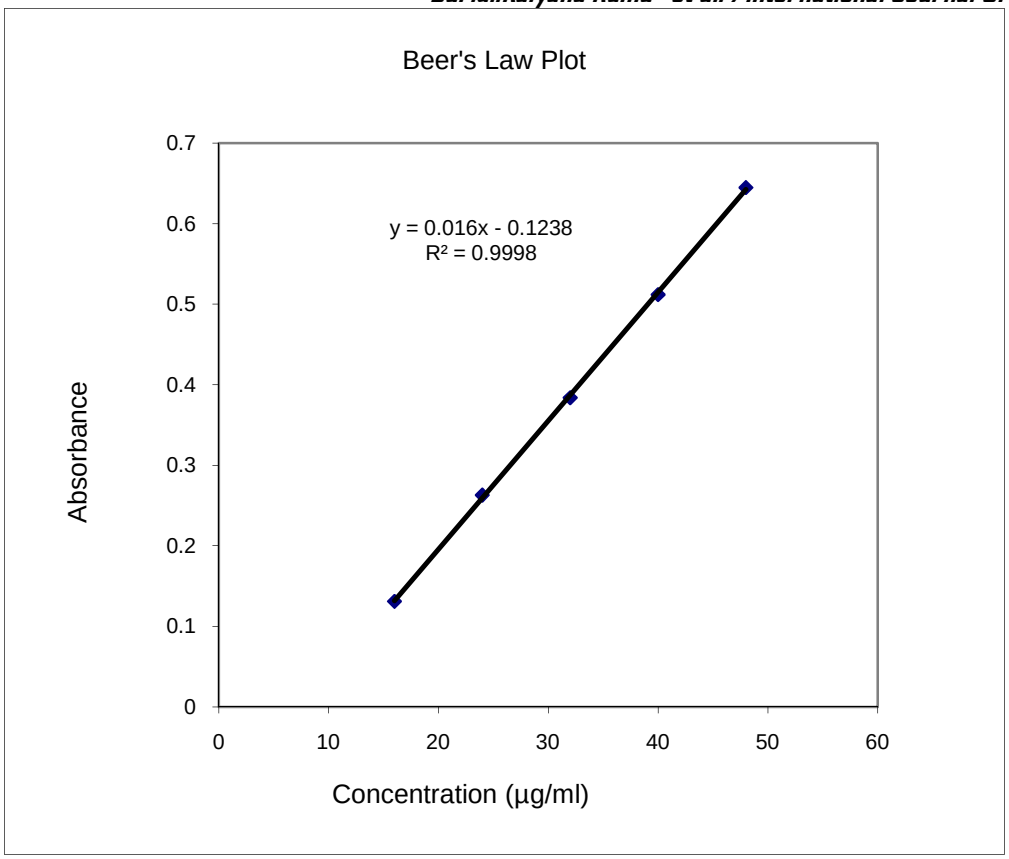

Figure-3 Showing Calibration Graph of SUM-CTC

5. RESULTS AND DISCUSSIONS

In developing this method, a systematic study of the effects of various parameters were undertaken by varying one parameter at a time and controlling all others fixed. The effect of various parameters such as time, volume and strength of CTC reagent and pH buffer solution and solvent for final dilution of the colored species were studied and the optimum conditions were established. Among the various water immiscible organic solvents(C_6H_6 $CHCl_3$, di chloro methane, nitro benzene, chloro benzene and CCl_4)tested for the extraction of colored coordinate complex into organic layer, nitrobenzene was preferred for selective extraction of colored complex from organic phase.

The ratio of organic to aqueous phase was found to be 1:1.5 by Slope ratio method. 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) were calculated and the results are summarized in table-1.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 are shown in Table-1.

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

Parameter	**Values**
λ_{max} (nm)	629.4nm
Beer's law limit(µg/ml)	16 - 48
Sandell's sensitivity (µg/cm^2/0.001 abs. unit	0.104166667
Molar absorptivity (Litre/mole/cm)	3969.6
Regression equation (Y)*	
Intercept (a)	-0.123
Slope(b)	0.016
%RSD	0.89978
% Range of errors(95% Confidence limits)	
0.05 significance level	0.9444
0.01significance level	1.4811

*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. The ingredients usually present in formulations of SUM did not interfere with the proposed analytical method.

Table-2: Analysis of sumatriptan succinate by proposed and reference methods.

Method	*Formulations	Labeled Amount (mg)	Found by Proposed Methods			Found by Reference Method ± SD	#% Recovery by Proposed Method ± SD
			**Amount found ± SD	t	f		
CTC	Tablet-1	50	49.683± 0.061	0.957	4.189	49.647 ±0.125	99.365± 0.122
	Tablet-2	50	49.708 ± 0.079	0.116	4.517	49.702± 0.169	99.41 7± 0.159

* Different tablets 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 distilled water (λ_{max}=220nm).

Chemistry of colored species: The color species formed is the coordination complex of the drug (electron donor) and the central metal of cobalt thiocyanate, which is extractable into nitro benzene from aqueous solution. Formation of the green colored complex when SUM was treated with CTC is due to the presence of the tertiary amino group in it. It is based on the analogy of tertiary amine as given in scheme (Fig-4).

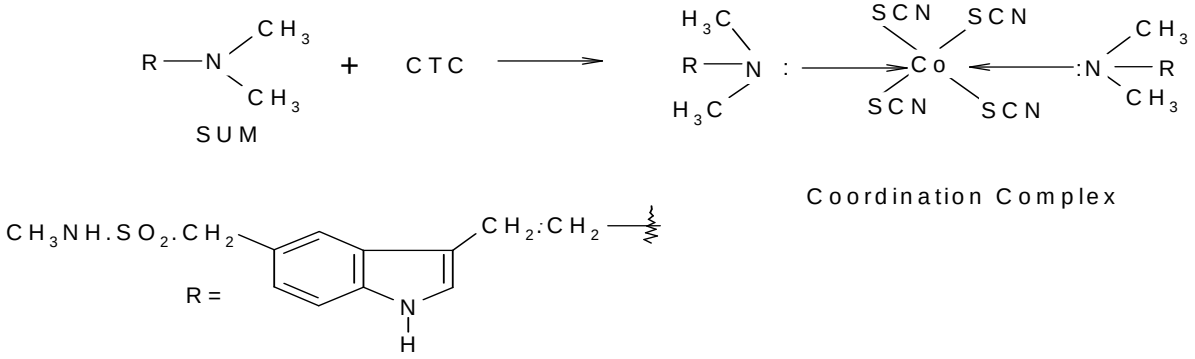

Figure-4: Showing the scheme

6. CONCLUSION

The reagents utilized in the proposed method are cheap, 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.

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