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Research Article

Use of Charge Transfer Complexation Reactions for the Spectrophotometric Determination of Sumatriptan in Pharmaceuticals

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Studies were carried out to use the charge-transfer reactions of sumatriptan (SMT), extracted from neutralized sumatriptan succinate (STS), as n-electron donor with the π-acceptor, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and σ-acceptor, and iodine (I_2). The formation of the colored complexes was utilized for the development of simple, rapid, and accurate spectrophotometric methods for the determination of SMT in pure form as well as in its tablets. The quantification of colored products was made spectrophotometrically at 585 nm for the CT complex formed between SMT and DDQ (DDQ method) and at 375 nm for the CT complex formed between SMT and I_2 (I_2 method). Beer's law is obeyed over the concentration ranges of 4.0–56.0 μg mL^{-1} and 2.0–28.0 for DDQ and I_2, respectively, with correlation coefficients *(r)* of 0.9997 and 0.9998. The analytical parameters such as apparent molar absorptivity, Sandell's sensitivities, and limits of detection (LOD) and quantification (LOQ) are also reported for both methods. The described methods were successfully applied to the determination of SMT in tablets. No interference was observed from the common excipients present in tablets. The reaction stoichiometry in both methods was evaluated by Job's method of continuous variations and was found to be 1 : 1 (donor : acceptor).

1. Introduction

Triptans are a group of tryptamine-based drugs used in the acute treatment of migraine headaches. Sumatriptan succinate (Figure 1) is one among them and is structurally related to the neurotransmitter serotonin. Sumatriptan succinate (STS) is a 5-hydroxytryptamine (5-HT) receptor subtype (a member of the 5-HT 1D family) having only a week affinity for 5-HT_{1A}, 5-HT_{5A}, and 5-HT_7 receptors and chemically designated as [3-[2-(Dimethylamino)ethyl]-1H-indol-5-yl]-N-methylmethanesulfonamide hydrogen butanedioate [1]. STS acts by selectively binding to serotonin type-1D receptors (serotonin agonist) and rapidly terminates a migraine attack while eliminating associated symptoms such as nausea, vomiting, and light and sound sensitivity [2].

STS has official monographs in British pharmacopeia (BP) [1], European pharmacopeia (EP) [3], and United States pharmacopeia USP [4] which describe liquid chromatographic methods for the assay of STS. From the literature survey, it is found that high performance liquid chromatography (HPLC) has been used for the assay of STS in human plasma [5, 6], human serum [7], rabbit plasma [8] and human plasma, and urine [9] whereas liquid chromatography-mass spectrophotometry (LC-MS/MS) in body fluids [10] and human plasma [11]. Several methods have been reported for the determination of STS in pharmaceuticals and include UV spectrophotometry [12–16], HPLC [17–20], ultraperformance liquid chromatography (UPLC) [21], high performance thin layer chromatography (HPTLC) [16, 22], capillary electrophoresis [23], micellar electrokinetic chromatography [24], and voltammetry [25–27].

Besides, SMT in pharmaceuticals is reported to have been determined by visible spectrophotometry employing

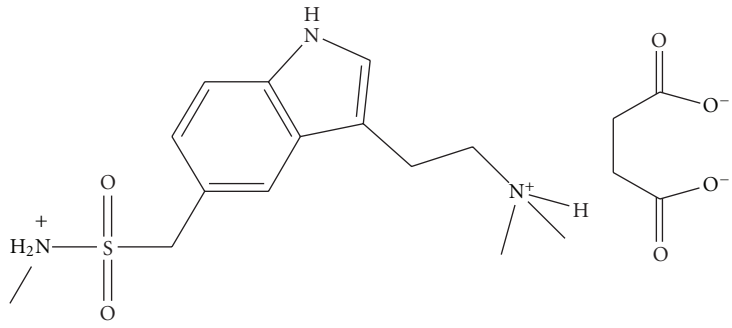


Figure 1: Structure of sumatriptan succinate.

different reaction schemes. Satyanarayana and Rao [28] have described two methods using *in situ* bromine, methyl orange, and indigo carmine as reagents. Based on a well-known redox reaction and employing Folin-Ciocalteu's reagent [22], the drug in pharmaceutical dosage forms was determined byTipre and Vavia . Chloranil and acetaldehyde [29] were used as reagents for the assay of SMT based on condensation reaction. Using acetaldehyde in combination with sodium nitroprusside and based on inner molecular complex formation, the drug was assayed by Kalyanaramu and Raghubabu [30]. The drug is reported to undergo oxidative coupling reaction in the presence of brucine and sodium metaperiodate based on which method was developed by Kalyanaramu and Raghubabu [31]. The reaction between SMT and sodium salt of 1,2-naphthaquinone-4-sulphonic acid (Folin reagent) yielded a brown colored chromogen [32] forming the basis for the assay of the drug. A green-colored ternary complex formed by the drug with cobalt-thiocyanate was extracted into benzene and measured at 630 nm and served as the basis of its assay [33]. Tropaeolin OOO is reported to form chloroform extractable orange-colored ion pair with SMT having an absorption maximum at 483 nm, and this was used for the sensitive assay of the drug by Kalyana Ramu and Raghubabu [34].

Molecular interactions between electron donors and acceptors are generally associated with the formation of intensely colored charge-transfer (CT) complexes which absorb radiation in the visible region [35, 36].

The reported visible spectrophotometric methods suffer from one or more disadvantages such as rigid pH control, heating and/or extraction step, use of multistep reaction/s or concentrated acids, longer contact time, less stable colored species, and narrow linear dynamic range as indicated in Table 1.

Based on C-T complexation reactions, SMT has been assayed in pharmaceuticals employing p-chloranilic acid [37] and 2,3,5,6-tetrachloro-p-benzoquinone [29] as π-acceptors. Substituted quinine such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (a π-acceptor) and iodine (I_2) (a σ-acceptor) have earlier been used as C-T complexing agents for the spectrophotometric assay of several pharmaceuticals [38–40]. However, these reagents have not been applied for the spectrophotometric assay of SMT.

In the present work, attempts have been made to assay SMT (donor) in pure drug and in tablets through C-T complexation with DDQ and iodine as acceptors. These methods have been demonstrated to be simple, rapid, and free from drastic experimental conditions and have wide linear dynamic ranges and are more sensitive than many reported methods (Table 1).

2. Experimental

2.1. Instrument. A Systronics model 106 digital spectrophotometer (*Systronics,* Ahmedabad, Gujarat, India) provided with 1 cm matched quartz cells was used for all absorbance measurements.

2.2. Reagents and Materials. All the reagents and solvents were of analytical-reagent grade, and distilled water obtained from Crysta-500 water purification system was used throughout the investigation. Sumatriptan succinate sample (purity 99.5%) was kindly supplied by MSN laboratories, Hyderabad, India.

2,3-Dichloro-5,6-Dicyano-1,4-Benzoquinone (DDQ). A 0.1% (w/v) DDQ solution was prepared by dissolving 100 mg of the chemical (Avra Synthesis Pvt. Ltd., Hyderabad, India) in 1,4-dioxane (Merck, Mumbai, India) and diluted to the mark with same solvent in 100 mL calibrated flask. It was prepared afresh just before use.

Iodine Solution (I_2). A 0.5% (w/v) I_2 solution was prepared by dissolving 0.5 g of the pure resublimed iodine (S.D. Fine Chem Ltd, Mumbai, India) in 100 mL of dichloromethane and used after 30 min for the assay.

Sodium Carbonate (10%). A 10% (w/v) solution was prepared in water.

Standard Sumatriptan Base (SMT) Solution. Twenty-eight milligrams of pure sumatriptan succinate (STS) was dissolved in about 20 mL of water, and the solution was quantitatively transferred into a 125 mL separating funnel containing 10 mL of 10% sodium carbonate (pH 8.6). Complete extraction of SMT base was achieved at this

Table 1: Comparison of the proposed and the existing visible spectrophotometric methods.

Sl. no.	Reagent/s	λ_{max}, nm	Beer's law range, $\mu g\,mL^{-1}$ (ε in $l\,mol^{-1}\,cm^{-1}$)	Remarks	Reference
1	Bromate-bromide- (a) methyl orange,	508	0.2–1.6 (1.90×10^5)	Multistep reaction, time consuming	[28]
	(b) indigo carmine	610	2.0–12.0 (2.71×10^4)		
2	Folin-Ciocalteu reagent	760	2.0–6.0 —	Multi step reaction	[22]
3	(a) Quinone	548	5.0–25.0 (1.00×10^4)	Involves heating step, time consuming	[29]
	(b) acetaldehyde with p-chloranil	660	20.0–60.0 (3.19×10^4)		
4	Sodium nitroprusside acetaldehyde	552	4.0–20.0 (1.10×10^4)	Requires rigid pH control	[30]
5	(a) Brucine-sodium metaperiodate,	520	4.0–20.0 —	Multi step reaction	[31]
	(b) citric acid-acetic anhydride	580	8.0–24.0 —		
6	Folin reagent	455.6	16.0–48.0 (3.85×10^3)	Strict pH control, time consuming	[32]
7	Cobalt thiocyanate	629.4	16.0–48.0 (3.97×10^3)	Involves extraction step	[33]
8	Tropaeolin-OOO	482.5	2.0–10.0 (2.08×10^4)	Requires rigid pH control; involves liquid-liquid extraction	[34]
9	p-Chloranilic acid	520	9.28×10^2	—	[37]
10	(a) 2,3-dichloro-5,6-dicyano-1,4-benzoquinone,	585	4.0–56.0 (4.77×10^3)	*Single step reaction, no heating or extraction step, or use of single reagent*	*Present methods*
	(b) iodine	375	2.0–28.0 (9.56×10^3)		

pH. The resulting base was extracted with 4×20 mL of chloroform. The two phases were allowed to separate, and the chloroform layer was dried over anhydrous sodium sulphate, the solvent was evaporated on a water bath, and the resulting sumatriptan base (SMT) was dissolved in acetonitrile for DDQ method and in dichloromethane for I_2 method; the volume was then completed to the mark with the respective solvents. The resulting solution (200 $\mu g\,mL^{-1}$ in sumatriptan base) was diluted appropriately with acetonitrile to get a working concentration of 80 $\mu g\,mL^{-1}$ SMT for use in DDQ method and with dichloromethane to get a working concentration of 40 $\mu g\,mL^{-1}$ SMT for use in I_2 method.

2.3. Assay Procedures

2.3.1. DDQ Method. Aliquots (0.25, 0.5, 1.0, ..., 3.5 mL) of a standard SMT (80 $\mu g\,mL^{-1}$) solution were accurately transferred into a series of 5 mL calibrated flasks, and the total volume was adjusted to 3.5 mL by adding adequate quantity of acetonitrile to each flask. One milliliter of 0.1% DDQ solution was added to each flask, the mixture was diluted to the volume with acetonitrile, and the absorbance of each solution was measured at 585 nm against a reagent blank at room temperature.

2.3.2. I_2 Method. Varying aliquots of standard SMT solution equivalent to 2.0–28.0 $\mu g\,mL^{-1}$ (0.2–3.5 mL of 40 $\mu g\,mL^{-1}$) were accurately measured and transferred into a series of 5 mL calibrated flasks, and 1 mL of 0.5% iodine solution was added to each flask, the content was mixed well, and the flasks were allowed to stand at room temperature for 10 min. The volume was brought up to the mark with dichloromethane, and the absorbance was measured at 375 nm against a reagent blank similarly prepared without adding SMT base solution at room temperature.

Standard graph was prepared by plotting the absorbance *versus* drug concentration, and the concentration of the unknown was read from the calibration graph or computed from the respective regression equation.

2.3.3. Procedure for Tablets. Ten tablets each containing 25 or 50 mg of SMT were weighed and finely powdered. An accurately weighed amount of the powder equivalent to 28.0 mg of STS was dissolved in about 30 mL distilled water

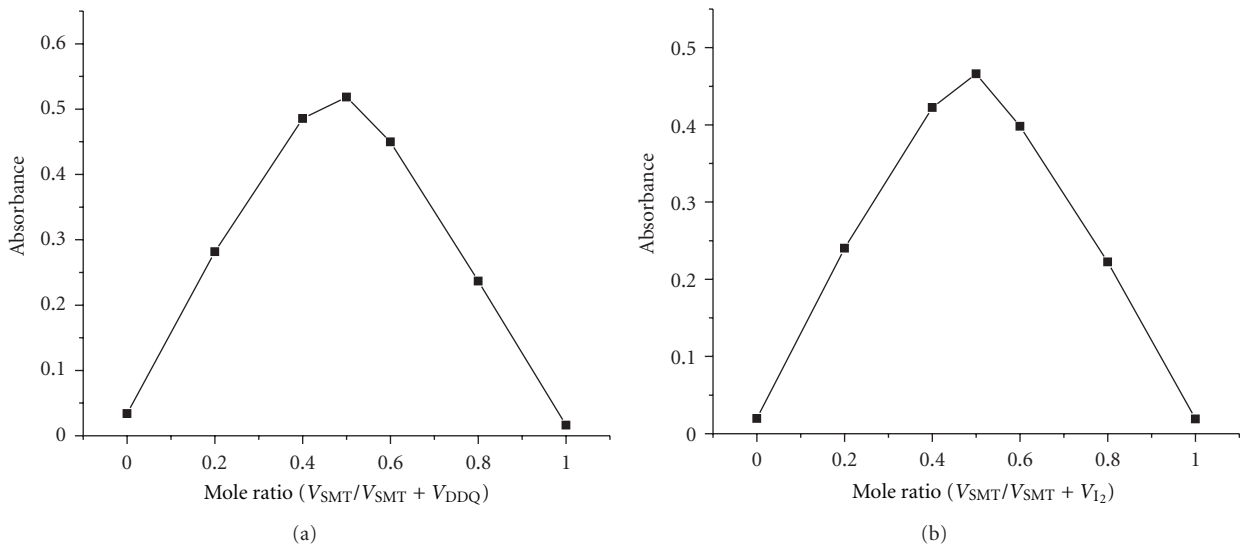


Figure 2: Jobs Plot: (a) DDQ method, (b) I_2 method.

in a 50 mL calibrated flask. The mixture was shaken for 10 min and filtered using Whatman No. 42 filter paper into a 125 mL separating funnel containing 10 mL of 10% sodium carbonate. The base was extracted as described under "Standard sumatriptan base solution." The base solution (i.e., 200 μg mL^{-1} SMT) was diluted appropriately to get 80 and 40 μg mL^{-1} and assayed by the DDQ method and I_2 method, respectively.

2.3.4. Procedures for Selectivity Study. A placebo blank of the composition: talc (15 mg), starch (30 mg), lactose (15 mg), glucose (15 mg), sodium citrate (5 mg), magnesium stearate (20 mg), calcium gluconate (20 mg) and sodium alginate (5 mg), was made, and its solution was prepared in 50 mL calibration flask as described under procedure for tablets and then subjected to analysis following the procedures described previously.

To 10 mg of the placebo blank of the composition described previously, 14 mg of STS was added and homogenized, transferred to a 50 mL calibrated flask, and the solution was prepared as described under procedure for tablets and then subjected to analysis by the recommended procedures described previously after appropriate dilution.

2.3.5. Composition of the C-T Complexes. The composition of the C-T complex was established by Job's method of continuous variations using equimolar concentrations of the drug (base form) and reagents (6.04×10^{-4} M in DDQ-method, 2.41×10^{-4} M in I_2-method). Five solutions containing SMT and the reagent (DDQ or I_2) in various molar ratios, with a total volume of 5 mL in both methods, were prepared. The absorbance of solutions was subsequently measured at 585 nm in DDQ-method and at 375 nm in I_2-method. The graphs of the results obtained (Figure 2) gave a maximum at a molar ratio of $X_{max} = 0.5$ in both methods which indicated the formation of a 1 : 1 C-T complex between SMT and reagent (DDQ or I_2). This is due to the steric hindrance of tertiary nitrogen and delocalization of electrons in nitrogen present in indole moiety; these nitrogens cannot act as n-donor. Thus, only secondary aliphatic nitrogen is vulnerable to charge-transfer complex formation.

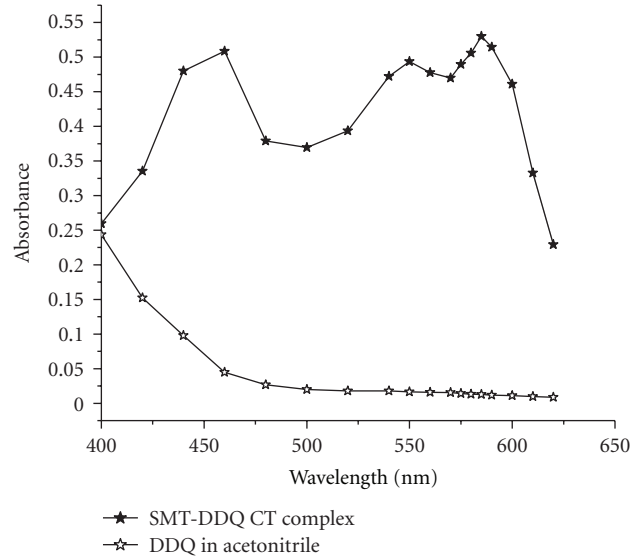


Figure 3: Absorption spectra (DDQ method).

3. Results and Discussion

3.1. Absorption Spectra. The reaction of DDQ as a π-acceptor with sumatriptan base as n-electron donor results in the formation of an intense reddish violet product which exhibits three maxima at 585, 550, and 460 nm (Figure 3). These bands can be attributed to the formation of DDQ radical anions arising from the complete transfer of n-electrons from donor to acceptor moieties in acetonitrile. The absorption band at 585 nm was selected as analytical wavelength keeping

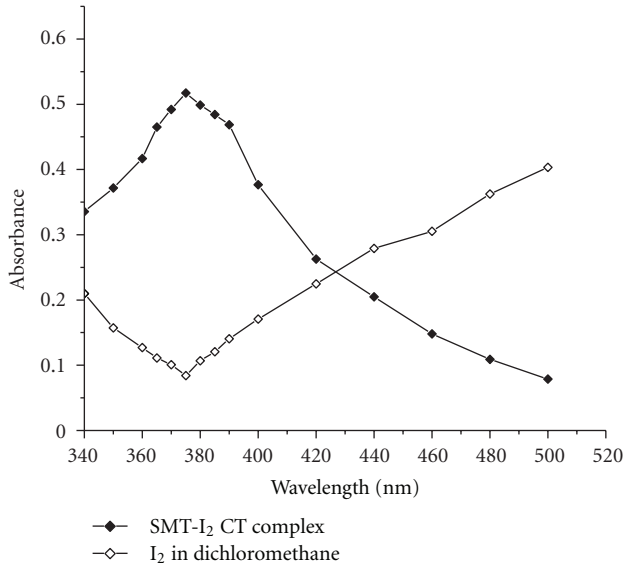


Figure 4: Absorption spectra (I_2 method).

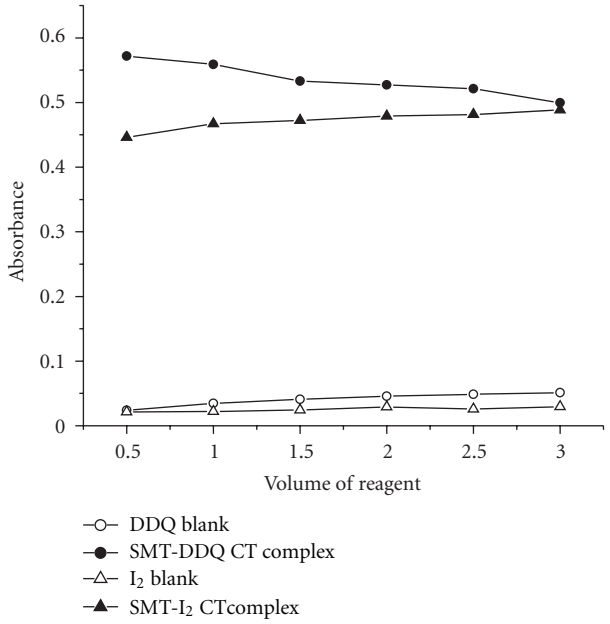


Figure 5: Effect of reagent concentration ($32\,\mu g\,mL^{-1}$ SMT in method A and $16\,\mu g\,mL^{-1}$ SMT in method B).

in view the sensitivity of the reaction product and blank absorbance (Figure 3). Similarly, the reaction of SMT with I_2 results in the formation of a yellow product which exhibits an absorption maximum 375 nm (Figure 4).

3.2. Reaction Pathway

3.2.1. Reaction with π-Acceptor (DDQ). The chemistry involved in the proposed DDQ-method is based on the reaction of the basic nitrogen of SMT as n-donor with the π-acceptor DDQ to form charge transfer complex which subsequently dissociates into radical anions depending on the polarity of the solvent used. In polar solvents, such as acetonitrile, complete electron transfer from the donor to the acceptor moiety takes place with the formation of intensely colored radical anions [41], according to the following equation:

$$\ddot{\mathrm{D}} + \mathrm{A} \longrightarrow \underset{\substack{\text{charge transfer}\\ \text{complex}}}{[\ddot{\mathrm{D}} \longrightarrow \mathrm{A}]} \longrightarrow \mathrm{D}^{\cdot+} + \underset{\substack{\text{radical}\\ \text{anion}}}{\mathrm{A}^{\cdot-}}. \quad (1)$$

The dissociation of the (D → A) complex is promoted by the high ionizing power of the acetonitrile. In SMT only aliphatic secondary nitrogen can donate electrons; due to the steric hindrance of tertiary aliphatic nitrogen and delocalization of electrons on nitrogen present in indole moiety, these nitrogens cannot act as n-donor.

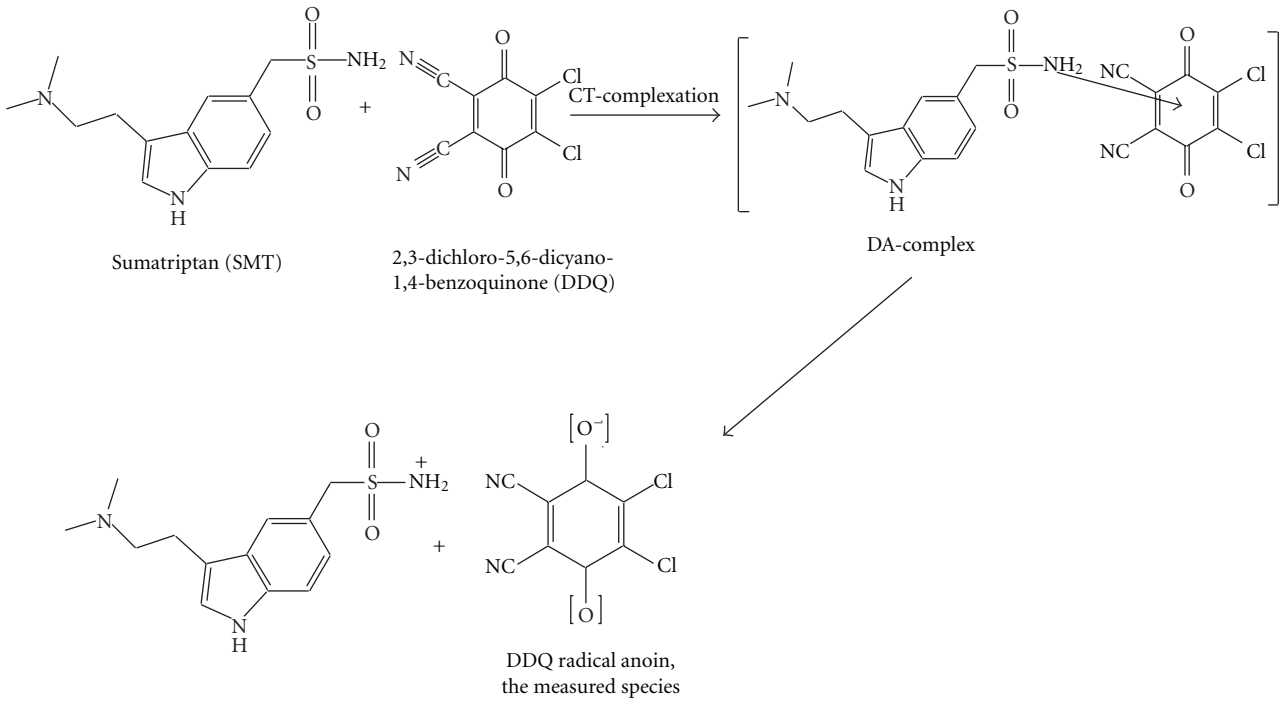
The salts of amines do not react with π-acceptor or σ-acceptor due to nonavailability of nonbonding electrons (n-electrons) on the nitrogen atom and insolubility in organic solvents. To determine amine salts, it is necessary to first neutralize the acid and then extract the amine into a nonaqueous solvent [42]. The tentative reaction pathway for SMT-DDQ complex is proposed and illustrated in Scheme 1.

3.2.2. Reaction with σ-Acceptor (Iodine). SMT, an n-donor (D), in dichloromethane forms a lemon yellow-colored C-T complex with iodine (I_2) σ-acceptor (A), and the resulting colored species was found to absorb maximally at 375 nm (Figure 4). The color of iodine in dichloromethane is violet showing absorption maximum (λ_{max}) at 500 nm. This color was changed into lemon yellow when mixed with drug. This change in color and the appearance of the peak were attributed to the formation of charge-transfer complex between SMT and iodine. The interaction between the donor and acceptor occurs according to Scheme 2.

3.3. The Effect of Different Experimental Variables

3.3.1. Effect of Reagents Concentration. The effect of the reagent concentration on the intensity of the color at the selected wavelengths was ascertained by adding different amounts of the reagents DDQ and I_2 to fixed concentrations of 32 and $16\,\mu g\,mL^{-1}$ SMT in DDQ-method and I_2-method, respectively. It was found that 1.0 mL each of 0.1% DDQ and 0.5% I_2 solutions were sufficient for the production of maximum and reproducible color intensity, and the highest absorbance remained unaffected by further addition of these reagents (Figure 5).

3.3.2. Effect of Solvent. In order to select a suitable solvent for preparation of the reagent solutions used in the study, the reagents were prepared separately in different solvents such as 1,4-dioxane, chloroform, acetonitrile, acetone, t-butanol,2-propanol, and dichloromethane, and the reaction of SMT with DDQ was followed; 1,4-dioxane was best suited for preparation of DDQ solution, and acetonitrile was suitable for preparation of drug. For the reaction between SMT and I_2, dichloromethane was found suitable for preparation of both SMT and I_2.



Scheme 1: The tentative reaction mechanism for SMT-DDQ complex formation.

Table 2: Regression and analytical parameters.

Parameter	DDQ method	I_2 method
λ_{max}, nm	585	375
Beer's law limits (μg mL^{-1})	4.0–56.0	2.0–28.0
Molar absorptivity (L mol^{-1} cm^{-1})	4.77×10^3	9.56×10^3
Sandell sensitivity* (μg cm^{-2})	0.0620	0.0309
Limit of detection (μg mL^{-1})	0.77	0.17
Limit of quantification (μg mL^{-1})	2.32	0.52
Regression equation, Y**		
Intercept, (a)	−0.0104	0.0198
Slope, (B)	0.0170	0.0295
Correlation coefficient (r)	0.9997	0.9998
Standard deviation of intercept (S_a)	0.00714	0.00499
Standard deviation of slope (S_b)	0.00021	0.00029

* Limit of determination as the weight in μg per mL of solution, which corresponds to an absorbance of $A = 0.001$ measured in a cuvette of cross-sectional area 1 cm^2 and l = 1 cm. ** $Y = a + bX$, where Y is the absorbance, a is the intercept, b is the slope, and X is the concentration in μg mL^{-1}.

Table 3: Evaluation of intraday and interday precision and accuracy.

Method	SMT taken (μg mL^{-1})	Intra-day ($n = 7$)			Inter-day ($n = 5$)		
		SMT found[a] (μg mL^{-1})	%RSD[b]	%RE[c]	SMT found[a] (μg mL^{-1})	%RSD[b]	%RE[c]
DDQ method	16.0	16.4	0.90	2.27	16.4	1.20	2.63
	32.0	32.4	0.93	1.29	32.5	1.25	1.63
	48.0	47.6	1.79	0.83	47.4	1.93	1.16
I_2 method	8.00	7.91	1.71	1.09	7.90	1.91	1.22
	16.0	16.3	0.82	1.98	16.3	1.06	2.16
	24.0	24.2	1.72	0.93	24.3	2.01	1.07

[a] Mean value of five determinations; [b] relative standard deviation (%); [c] relative error (%).

Table 4: Robustness and ruggedness.

Method	SMT taken, μg mL^{-1}	Method robustness Parameters altered		Method ruggedness	
		Reagent volume, mL[a] RSD, % ($n = 3$)	Reaction time[b] RSD, % ($n = 3$)	Interanalysts RSD, % ($n = 4$)	Intercuvettes RSD, % ($n = 4$)
DDQ method	16.0	1.23	0.93	1.56	1.34
	32.0	0.89	1.15	1.31	1.47
	48.0	1.11	1.49	1.78	1.50
I_2 method	8.00	1.02	0.85	1.40	1.29
	16.0	1.18	1.32	1.63	1.09
	24.0	1.40	1.28	1.75	1.13

[a] In both methods, the volume of reagent was 0.8, 1.0, and 1.2 mL. [b] The reaction time was 4, 5, and 6 min in DDQ method and 9, 10, and 11 min in I_2 method.

Table 5: Results of analysis of tablets by the proposed methods.

Tablet brand name	Label claim mg/tablet	Found (percent of label claim ± SD)[a]		
		Reference method	Proposed methods	
			DDQ method	I_2 method
Suminat-25	25	101.1 ± 0.83	102.1 ± 1.09	99.11 ± 1.35
			$t = 1.63$	$t = 2.81$
			$F = 1.72$	$F = 2.64$
Suminat-50	50	99.43 ± 1.05	101.3 ± 1.80	100.9 ± 1.67
			$t = 2.01$	$t = 1.67$
			$F = 2.94$	$F = 2.53$

[a] Mean value of five determinations.
Tabulated t-value at the 95% confidence level is 2.78.
Tabulated F-value at the 95% confidence level is 6.39.

Similarly, the effect of the diluting solvent was studied for both methods, and the results showed that the ideal diluting solvent to achieve maximum sensitivity and stability of the colored species was acetonitrile in DDQ-method and dichloromethane in I_2-method.

3.3.3. Effect of Reaction Time and Stability of the C-T Complexes. The optimum reaction time was determined by following the color development upon the addition of reagent solution to the SMT solution at room temperature. Complete color development was attained after 5 min with DDQ while the reaction with I_2 requires 10 min for complete color development. The absorbance of these radical anions remained stable for at least 2 hrs and 50 min for DDQ-method and I_2-method, respectively.

3.4. Molar Ratio of the Reaction. Job's continuous variations graph for the reaction between SMT and DDQ or I_2 (Figure 2) shows that the interaction occurs on an equimolar basis *via* the formation of charge-transfer complexes 1 : 1 (SMT : reagent). This finding was anticipated by the presence of more basic or electron donating centre (–NH) in the SMT.

3.5. Method Validation

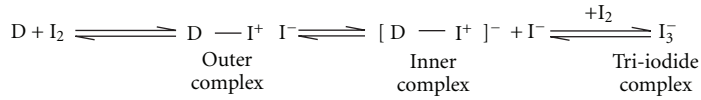
3.5.1. Linearity and Sensitivity. Under optimum experimental conditions for determination of the drug under study, the absorbance *versus* concentration plots was found to be linear over the concentration ranges 4.0–56.0 μg mL^{-1} in DDQ-method and 2.0–28.0 μg mL^{-1} as shown in Table 2. The regression parameters calculated from the calibration graphs data, along with the standard deviations of the slope (S_b) and the intercept (S_a), are presented in Table 2. The linearity of the calibration graphs was demonstrated by the high values of the correlation coefficient (r) and the small values of the y-intercepts of the regression equations. The molar absorptivity and Sandell sensitivity of the methods A and B were also shown in Table 2. Sensitivity of the methods can be determined, through the limit of detection (LOD) and limit of quantification (LOQ) which were calculated and recorded in Table 2.

3.5.2. Precision and Accuracy. In order to determine the precision of the proposed methods, solutions containing three different concentrations of SMT were prepared and analyzed in seven replicates, and the analytical results were summarized in Table 3. The low values of the relative standard deviation (% R.S.D) and percentage relative error

Table 6: Results of recovery study by standard addition method.

Tablets studied	DDQ method				I_2 method			
	SMT in tablets, μg mL^{-1}	Pure SMT added, μg mL^{-1}	Total found, μg mL^{-1}	Pure SMT recovered*, percent ± SD	SMT in tablets, μg mL^{-1}	Pure SMT added, μg mL^{-1}	Total found, μg mL^{-1}	Pure SMT recovered*, percent ± SD
Suminat-25	16.34	8.00	24.47	101.6 ± 1.22	7.93	4.00	12.00	101.8 ± 2.31
	16.34	16.0	32.17	98.94 ± 1.75	7.93	8.00	16.00	100.9 ± 1.19
	16.34	24.0	40.86	102.2 ± 0.78	7.93	12.0	19.77	98.67 ± 0.75
Suminat-50	16.21	8.00	24.32	101.4 ± 1.66	8.07	4.00	12.02	98.75 ± 1.32
	16.21	16.0	31.98	98.56 ± 1.13	8.07	8.00	16.20	101.6 ± 2.02
	16.21	24.0	39.38	99.00 ± 0.98	8.07	12.0	20.37	102.5 ± 1.06

* Mean value of three determinations.



Scheme 2: Reaction pathways for the formation of electron donor-acceptor complex and radical ion between SMT and iodine.

(% R.E) indicate the high precision and the good accuracy of the proposed methods. RSD (%) and RE (%) values were obtained within the same day to evaluate repeatability (intra-day precision) and over five days to evaluate intermediate precision (interday precision).

3.5.3. Selectivity. The selectivity of the proposed methods for the analysis of SMT was evaluated by placebo blank and synthetic mixture analyses. The recommended procedures were applied to the analysis of placebo blank, and the resulting absorbance readings in both methods were the same as those of the reagent blank, confirming no interference from the placebo. The analysis of synthetic mixture solution prepared as described earlier yielded percent recoveries of 98.3 ± 2.13 and 101.4 ± 1.91 ($n = 5$) for method A and method B, respectively. The results of this study showed that the inactive ingredients did not interfere in the assay indicating the high selectivity of the proposed methods and its utility for routine determination in pure drug and in tablets form.

3.5.4. Robustness and Ruggedness. To evaluate the robustness of the methods, two important experimental variables, volume of reagent and reaction time in both methods, were altered incrementally, and the effect of this change on the absorbance of the C-T complexes was studied. The results of this study are presented in Table 4 and indicated that the proposed methods are robust. Method ruggedness was evaluated by performing the analysis following the recommended procedures by four different analysts and on four different cuvettes by the same analyst. From the % RSD values presented in Table 4, one can conclude that the proposed methods are rugged.

3.5.5. Applications to Analysis of Tablets. The proposed methods were successfully applied to the determination of SMT in two representative tablets suminat-25 and suminat-50. The results obtained are showed in Table 5 and were compared with those obtained by the official method [12] by means of Student's *t*- and *F*-tests at 95% confidence level. The published reference method describes UV-spectrophotometric method for detection of STS in tablet formulation at 220 nm. In both cases, the average results obtained by the proposed methods and official method were statistically identical, as the difference between the average values had no significance at 95% confidence level with respect to accuracy and precision.

3.5.6. Recovery Study. To further ascertain the accuracy of the proposed methods, recovery experiment was performed *via* standard addition technique. To a fixed and known amount of SMT in tablet powder (preanalyzed), pure SMT was added at three concentration levels (50%, 100%, and 150% of the level present in the tablet), and the total was measured by the proposed methods. The determination with each concentration was repeated three times, and the results of this study presented in Table 6 indicated that the various excipients present in the formulations did not interfere in the assay, thereby further confirming the accuracy of the methods.

4. Conclusions

Two simple, sensitive, extraction-free, rapid, and cost-effective spectrophotometric methods based on charge transfer complex formation reactions were developed and validated for the determination of SMT. These suggested methods utilize a single-step reaction and single solvent. The methods are free from interferences from the common excipients and additives. The statistical parameters and the recovery data reveal good accuracy and precision of the methods. These methods, which can be used as general methods for the determination of SMT in bulk powder and dosage form, have many advantages over the separation

techniques, for example, HPLC, such as reduced cost, and speed with high accuracy. Moreover, these proposed methods have wide dynamic linear range than many of the previously reported methods as can be seen from Table 1. Hence, the proposed methods can be used in the routine analysis of drugs in quality control laboratories as spectrophotometers are available in all quality control laboratories and they involve very simple procedures.

Conflict of Interests

The authors do not have any conflict of interests with the commercial identities mentioned in the paper.

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