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Basavaiah, Kanakapura; Ramakrishna, Veeraiah; Somashekar, Chikkaswamy; Anil Kumar, Urdigere R.

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Sensitive and rapid titrimetric and spectrophotometric methods for the determination of stavudine in pharmaceuticals using bromate-bromide and three dyes

KANAKAPURA BASAVAIAH[1], VEERAIAH RAMAKRISHNA[2], CHIKKASWAMY SOMASHEKAR[1] and URDIGERE R. ANIL KUMAR[1]

[1]Department of Chemistry, University of Mysore, Manasagangotri, Mysore, 570006, India
[2]Department of Drugs Control, Government College of Pharmacy, Bangalore, 560027, India

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ABSTRACT

Four sensitive and rapid methods for the determination of stavudine (STV) in bulk drug and in dosage forms were developed and optimized. In titrimetry, aqueous solution of STV was treated with a known excess of bromate-bromide in HCl medium followed by estimation of unreacted bromine by iodometric back titration. Spectrophotometric methods involve the addition of a measured excess of bromate-bromide in HCl medium and subsequent estimation of the residual bromine by reacting with a fixed amount of methyl orange, indigocarmine or thymol blue followed by measurement of absorbance at 520 nm (method A), 610 nm (method B) or 550 nm (method C). In all the methods, the amount of bromate reacted corresponds to the amount of STV. Calculations in titrimetry were based on a 1:0.666 (STV : $KBrO_3$) stoichiometry and the method was found to be applicable over 3.5-10 mg range. A linear increase in absorbance with concentration of STV was observed in the spectrophotometric methods, and the Beer's law was obeyed over the concentration ranges 0.125-1.75, 1-10 and 1-9.0 μg mL^{-1} STV for method A, method B and method C, respectively. The methods when applied to the determination of STV in tablets and capsules were found to give satisfactory results.

Key words: Stavudine determination, titrimetry, spectrophotometry, bromate-bromide, dyes, pharmaceuticals.

INTRODUCTION

Stavudine (STV), chemically known as 2^1-3^1-didehydro-2^1-3^1-dideoxythymidine (Fig. 1), is a nucleoside analog reverse transcriptase inhibitor (NARTI) active against HIV (The Merck Index 1996). STV is converted intracellularly to triphosphate which stops the DNA synthesis of retroviruses through competitive inhibition of reverse transcriptase and incorporation into viral DNA. It is the fourth antiretroviral drug in the market and is used in the treatment of HIV infection. The drug is official in United States of Pharmacopoeia (The United States Pharmacopoeia 2006). which describes high performance liquid chromatography as assay procedures for bulk drug and tablets, respectively.

Correspondence to: Basavaiah K.
E-mail: basavaiahk@yahoo.co.in

A number of methods based on high performance liquid chromatography (Bazy et al. 2005, Verweij-van Wissen et al. 2005, Contreras et al. 2004), liquid chromatography-tandem mass spectrometry (Compain et al. 2005, Huang et al. 2004, Raices et al. 2003, Fan et al. 2002, Wiesner et al. 2002), micellar electrokinetic chromatography (Fan and Stewart 2002), radio immuno assay (Tran et al. 2003) and electrophoresis (Pereira et al. 2005) are known for the quantitative determination of STV in biological matrices such as blood plasma, blood serum and human cells. Several chromatographic techniques including HPLC (Dunge et al. 2005, Djurdjevic et al. 2004, Zhang et al. 2003, Sablon et al. 2004, Pai and Desai 2003, Rezk et al. 2003), HPTLC (Wankhede et al. 2005, Kaul et al. 2005) and LC-MS (Volosov et al. 2002), have been used for the determi-

nation of STV in pharmaceuticals. The drug has also been assayed by mass spectrometry (Soldin 2004) and UV-spectrophotometry (Sankar et al. 2002a).

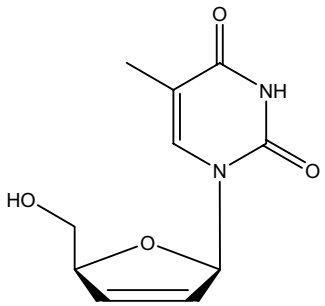

Fig. 1 – Structure of drug.

Despite its long history and established versatility, no titrimetric method has yet been reported for the determination of STV in pharmaceuticals. Visible spectrophotometry, because of its simplicity, speed, sensitivity, reasonable accuracy and precision, and cost-effectiveness, continues to be the preferred technique in laboratories of developing and underdeveloped nations, which can illafford expensive chromatographic and related techniques. Three procedures (Sarma et al. 2002a) have been reported for the assay of STV in pharmaceuticals using $KMnO_4$-Fast green FCF, permanganate/periodate-MBTH and iron(III)chloride-ferricyanide as reagents. The same authors (2002b) have used three more reagents, NBS-celestine blue, cobalt thiocyanate and ammonium molybdate for the spectrophotometric determination of STV. A method based on oxidative-coupling reaction (Sankar et al. 2002b) involving the use of iron (III)-MBTH is also found in the literature. But, these methods suffer from one or the other disadvantage like poor sensitivity, heating or extraction step and/or use of expensive chemical/organic solvent.

This paper reports the use of bromate-bromide reagent and three dyes-methyl orange, indigocarmine and thymol blue for rapid and sensitive determination of STV. The methods are based on the bromination/oxidation of the drug by *in situ* generated bromine followed by estimation of residual bromine by either iodometric back titration or by reacting with a fixed quantity of dye and measuring the change in absorbance. The methods on applying to tablets and capsules yielded satisfactory results and were comparable with those of a reference method.

MATERIALS AND METHODS

Apparatus: A Systronics Model 106 digital spectrophotometer provided with matched 1-cm quartz cells was used for all absorbance measurements. All chemicals used were of analytical reagent grade and distilled water was used to prepare all solutions.

Reagents and standards: Bromate-bromide mixture (4 mmol L^{-1} $KBrO_3$ – 40 × 10^{-3}mmol L^{-1} KBr) was prepared by dissolving accurately weighed 0.668 g of $KBrO_3$ (Sarabhai M Chemicals, Baroda, India) and 4.76 g of KBr (Indian Drugs and Pharmaceuticals Ltd, Hydrabad, India) in water and diluting to 1 litre in a calibrated flask, and the reagent was used in titrimetric work. A 0.024 mol L^{-1} sodium thiosulphate solution was prepared by dissolving about 5.96 g of chemical (Sisco Chem. Industries, Mumbai, India) in 1 litre of water. A 10% potassium iodide solution was prepared by dissolving 10 g of salt (Merck Chemicals, Mumbai, India) in 100 mL of water. To prepare 1% starch indicator, 1 g of soluble starch (S.d. Fine Chem., Mumbai, India) was made into paste in water and poured into 100 mL boiling water, boiled for 1 min and cooled. For spectrophotometric investigations, a bromate-bromide solution equivalent 1000 μg mL^{-1} $KBrO_3$ and 10- fold excess of KBr was prepared by dissolving accurately weighed 100 mg of $KBrO_3$ and 1 g of KBr in water and diluting to the mark in a 100 mL calibrated flask. This was then diluted stepwise to obtain working concentrations of 10, 30 and 50 μg mL^{-1} $KBrO_3$ for use in method A, method B and method C, respectively. Concentrated hydrochloric acid (S.D. Fine Chem., Mumbai, India; sp. gr. 1.18) was diluted appropriately with water to get 5 mol L^{-1} for spectrophotometric work and it was diluted to get 2 mol L^{-1} for titrimetry. A 500 μg mL^{-1} methyl orange dye solution was first prepared by dissolving accurately weighed 58.8 mg of dye (S.D. Fine Chem., Mumbai, India, assay 85%) in water and diluting to 100 mL in a calibrated flask and filtered using glass wool. It was further diluted to obtain a working concentration of 50 μg mL^{-1}. A stock standard solution equivalent to 1000 μg mL^{-1} indigo carmine was first prepared by dissolving accurately weighed 112 mg of dye (S.D. Fine Chem., Mumbai, India, 90% dye content) in water and diluting to volume in a 100 mL calibrated flask. The solution was then diluted 5-fold to get the working concentration of 200 μg mL^{-1}. A

1000 μg mL^{-1} stock standard solution of thymol blue was first prepared by dissolving accurately weighed 100 mg of dye (Loba. Chemie. Mumbai. India, 100% dye content) in water and diluting to volume in a 100 mL calibrated flask. The solution was then diluted five fold to get the working concentration of 200 μg mL^{-1}.

Standard drug solution: Pharmaceutical grade STV was received from Cipla India Ltd., (99.8% pure), as gift and was used as received. A stock standard solution containing 1 mg mL^{-1} STV was prepared by dissolving accurately weighed 250 mg of pure drug in water and diluting to the mark in a 250 mL calibrated flask. This solution was used for titrimetric work, and for spectrophotometric work, the same was diluted appropriately with water to get a working concentration of 5 μg mL^{-1} for method A, and 20 and 40 μg mL^{-1} for method B and method C, respectively.

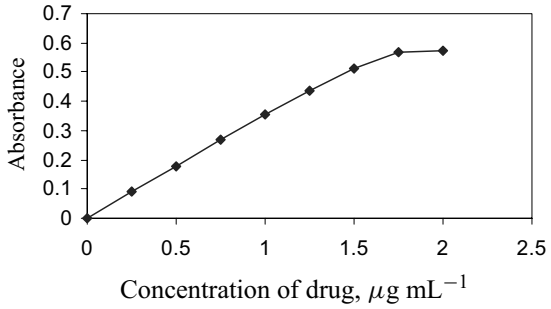

Fig. 2 – Beer's law curve for method A.

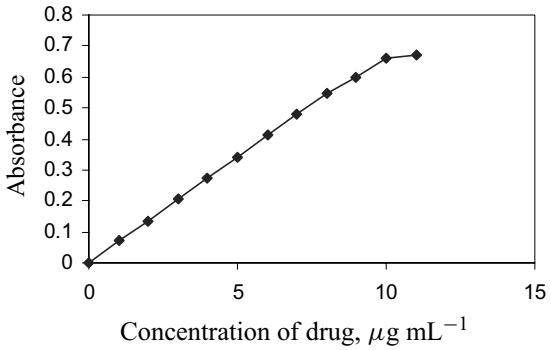

Fig. 3 – Beer's law curve for method B.

PROCEDURES

Titrimetry: A 10 mL aliquot of pure drug solution containing 3.5-10 mg of STV was accurately measured and

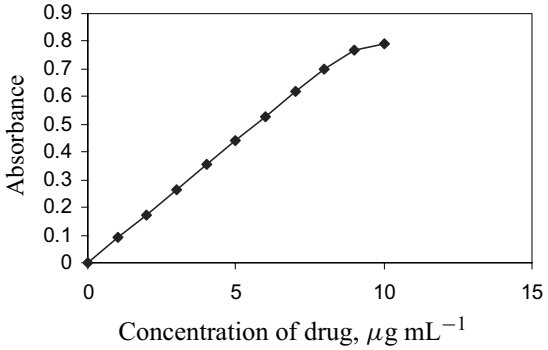

Fig. 4 – Beer's law curve for method C.

transferred into a 100 mL Erlenmeyer flask. The solution was acidified by adding 3 mL of 2 mol L^{-1} hydrochloric acid and diluted to 15 mL with water. Ten mL of bromate-bromide reagent (4 mmol L^{-1} w.r.t. $KBrO_3$) was pipetted into the flask, the flask was stoppered, the contents mixed and let stand for 10 min with occasional swirling. Finally, 5 mL of 10% potassium iodide solution was added, and the liberated iodine was titrated against 0.024 mol L^{-1} thiosulphate solution using starch as indicator towards the end point. A blank titration was performed, and the amount of drug in the measured aliquot was calculated from the amount of $KBrO_3$ reacted with drug.

Spectrophotometric method A: Different aliquots (0.25, 1.0, 1.5,... 3.5 mL) of a standard 5 μg mL^{-1} STV solution were transferred into a series of 10 mL calibrated flasks by means of a micro burette and the total volume was adjusted to 4 mL by adding adequate quantity of water. To each flask were added 1 mL each of 5 mol L^{-1} HCl and bromate-bromide solution (10 μg mL^{-1} in $KBrO_3$), the last being measured accurately. The flasks were stoppered, content mixed and let stand for 20 min with occasional shaking. Finally, 1 mL of 50 μg mL^{-1} methyl orange solution was added (accurately measured) and the volume was diluted to the mark with water and mixed well. The absorbance of each solution was measured at 510 nm against a reagent blank after 5 min.

Spectrophotometric method B: Varying aliquots (0.5,1.0, ... 5.0 mL) of a standard 20 μg mL^{-1} STV solution were transferred into a series of 10 mL calibrated flasks by means of a micro burette and the total

volume was brought to 5 mL by adding water. To each flask were added 1 mL of 5 mol L^{-1} hydrochloric acid and 1.5 mL of bromate-bromide solution (30 μg mL^{-1} in $KBrO_3$) by means of a micro burette. The content was mixed well and the flasks were kept aside for 10 min with intermittent shaking. Finally, 1 mL of 200 μg mL^{-1} indigo carmine solution was accurately measured and added to each flask, the volume was diluted to the mark with water, mixed well and absorbance measured against a reagent blank at 610 nm after 5 min.

Spectrophotometric method C: Different aliquots (0.25, 0.5, 1.0,... 2.25 mL) of a standard 40 μg mL^{-1} STV solution were transferred into a series of 10 mL calibrated flasks by means of a micro burette and the total volume was adjusted to 3 mL by adding adequate quantity of water. To each flask were added 1 mL each of 5 mol L^{-1} HCl and bromate-bromide solution (50 μg mL^{-1} in $KBrO_3$), the last being measured accurately. The flasks were stoppered, content mixed and let stand for 15 min with occasional shaking. Finally, 1 mL of 200 μg mL^{-1} thymol blue solution was added (accurately measured) and the volume was diluted to the mark with water and mixed well. The absorbance of each solution was measured at 550 nm against a reagent blank after 5 min.

In all the three spectrophotometric method, a standard graph was prepared by plotting the absorbance versus the concentration of STV. The concentration of the unknown was read from the calibration graph or computed from the regression equation derived using Beer's law data.

Procedure for Dosage Forms

Procedure for tablets/capsule: Twenty tablets/contents of capsules were weighed and ground into a fine powder. An amount of powder equivalent to 250 mg of STV was weighed into a 250 mL calibrated flask, 60 mL of water added and the mixture shaken for 20 min; then the volume was made up to the mark with water, mixed well and filtered using a Whatman No. 42 filter paper. First 10 mL portion of the filtrate was discarded and a suitable aliquot was then subjected to analysis by titrimetric method. The tablet extract (1 mg mL^{-1}) was diluted suitably with water to get working concentrations of 5, 20 and 40 μg mL^{-1} for method A, method B and method C, respectively before subjecting to analysis by spectrophotometric methods.

RESULTS AND DISCUSSION

The acidified solution of bromate and bromide behaves as an equivalent solution of bromine and has been widely used for the determination of many organic and inorganic substances. The present methods make use oxidising/brominating ability, and bleaching action of *in situ* generated bromine on the dyes used.

The proposed spectrophotometric methods are indirect and are based on the determination of the residual bromine (*in situ* generated) after allowing the reaction between STV and a measured amount of bromine to be complete. The bromine was determined by reacting it with a fixed amount of methyl orange, indigo carmine or thymol blue dye. The methods make use of bleaching action of bromine on the dyes, the decolouration being caused by the oxidative destruction of the dyes.

Method Development

Titrimetry: Direct titration of STV with *in situ* generated bromine was not successful. However, the reaction between the two was found to occur when the two were allowed to stand for some time, thus enabling the indirect titrimetric determination of STV. Hence, several factors like nature of acid and its concentration, reaction time, and the excess of reagent were optimized. Reproducible and stoichiometric results were obtained when 0.16 to 0.32 mol L^{-1} hydrochloric acid concentration was maintained. Hence, 0.24 mol L^{-1} acid concentration for the oxidation step and the iodometric back titration was used in the assay. Reaction was complete in 10 min and yielded stoichiometry of 1:0.666 (STV: $KBrO_3$), and contact times up to 20 min had no effect on the stoichiometry of the reaction. A constant molar-ratio was obtained when excess of reagent was not more than 2 times the theoretical amount. Under the optimum conditions, 3.5-10 mg of STV could be determined with good accuracy and precision with reaction stoichiometry of 1:0.666.

Spectrophotometry: STV, when added in increasing concentrations to a fixed concentration of *in situ* generated bromine, consumes the latter proportionally and there occurs a concomitant fall in the concentration of

bromine. When a fixed concentration of dye is added to decreasing concentrations of bromine, a concomitant increase in the concentration of dye results. Consequently, a proportional increase in the absorbance at the respective λ_{max} is observed with increasing concentration of STV.

Preliminary experiments were performed to fix the upper concentrations of the dyes that could be determined spectrophotometrically, and these were found to be 5, 20 and 20 μg mL^{-1} for methyl orange, indigo carmine and thymol blue respectively. A bromate concentration of 1 μg mL^{-1} in the presence of excess of bromide was found to bleach the red colour due to 5 μg mL^{-1} methyl orange whereas 4.5 and 5.0 μg mL^{-1} bromate was required to destroy the blue and violet colour due to 20 μg mL^{-1} each of indigocarmine and thymol blue, respectively. Hence, different concentrations of STV were reacted with 1 mL of 10 μg mL^{-1} $KBrO_3$ in method A, 1.5 mL of 30 μg mL^{-1} $KBrO_3$ in method B and 1 mL of 50 μg mL^{-1} $KBrO_3$ in method C respectively, followed by determination of residual bromine as described under the respective procedure.

For both steps, i.e., the reaction between STV and bromine, and the determination of the latter by reacting with the dye, HCl medium was found to be ideally suited. One mL of 5 mol L^{-1} acid in a total volume of about 5-7 mL was used in all the methods and the same quantity of acid was maintained for the bleaching step. Reaction times of 20, 10 and 15 min are not critical for method A, method B and method C. respectively, and any delay up to 30 min did not affect the absorbance reading. A 5 min standing time was found necessary for the complete bleaching of the dye colour by the residual bromine. The absorbance of each dye colour was constant for several hours even in the presence of reaction product.

Analytical data: A linear correlation was found between absorbance at λ_{max} and concentration of STV in the ranges given in Table I. The graphs showed negligible intercept as described by the regression equation:

$$Y = a + bX$$

(where Y = absorbance of 1-cm layer of solution; a = intercept; b = slope and X = concentration in μg mL^{-1}). Regression analysis of the Beer's law data using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficient (r) for each system and the values are presented in Table I. The optical characteristics such as Beer's law limits, molar absorptivity and Sandell sensitivity values of all the three methods are also given in Table I. The limits of detection (LOD) and quantitation (LOQ) calculated according to ICH guidelines (ICH Harmonised Triplicate Guideline 1996) are also presented in Table I and reveal the very high sensitivity of the methods.

Method validation: To evaluate the accuracy and intra-day precision of the methods, pure drug solution at three different levels (concentrations) was analysed, each determination being repeated seven times. The relative error (%) and relative standard deviation (%) were less than 3.0 and indicate high accuracy and precision of the methods (Table III). For a better picture of reproducibility on a day-to-day basis, a series of experiments was performed in which standard drug solution at three different levels was determined each-day for five days with all solutions being prepared afresh each day. The day-to-day relative standard deviation values were in the range of 2.0-3.5% and represent the best appraisal of repeatability of the proposed methods.

APPLICATION

Three brands of STV tablets/capsules in 30 and 40 mg strength are currently available in the Indian market. The validity of the methods was checked by applying them to assay in two brands of capsules and one brand of tablets. Table IV gives the results of assay and reveal that there is close agreement between the results obtained by the proposed methods and the label claim. The results were also compared statistically with those obtained by a literature method (Sankar et al. 2002a) by applying Student's t-test for accuracy and F-test for precision. At the 95% confidence level, the calculated t- and F-values did not exceed the tabulated values (t = 2.77 and F = 6.39) suggesting that the proposed methods are as accurate and precise as the literature method.

The accuracy and validity of the proposed methods were further ascertained by performing recovery experiments. Pre-analysed tablet/capsule powder was spiked with pure STV at three different levels and the total was found by the proposed methods. Each determination was repeated three times. The recovery of pure

TABLE I
Comparison of performance characteristics of proposed methods with the existing spectrophotometric methods.

Sl No.	Reagent*	λ_{max}, nm	Linear range, μg mL^{-1}	$\in$, L mol^{-1}cm^{-1}	Remarks	Ref.
1.	a) $KMnO_4$-FG FCF	640	1–8	1.28×10^4	Uses an oxidant, which is unstable in solution	Sarma et al. 2002a
	b) $NaIO_4$-MBTH	620	0.6–6.0	2.02×10^4	Use an expensive chemical	
	c) Iron (III)-ferricyanide	740	9.0–75.0	1.24×10^3		
2.	a) NBS-celestine blue	540	0.7–6.0	1.6×10^4	Uses an unstable solution	Sarma et al. 2002b
	b) Cobalt thiocyante	610	1.5–15.0	7.7×10^3	Involves extraction step with organic solvent	
	c) Ammonium molybdate	700	11–150	1.0×10^3	Requires heating; least sensitive	
3.	Iron (III)-MBTH					Sankar et al. 2002b
4.	a) BrO_3^--Br^--Methyl orange	520	0.125–1.75	3.94×10^4	No heating or	
	b) BrO_3^--Br^--Indigo carmine	610	1–10	1.45×10^4	extraction step, uses	Present methods
	c) BrO_3^--Br^--Thymol blue	550	1–9	1.99×10^4	stable solution	

*FGFCF = Fast green FCF; MBTH = 3-methylbenzothiazolinone hydrazone; NBS = N-bromosuccinimide.

TABLE II
Quantification and regression characteristics of spectrophotometric methods.

Parameter	Method A	Method B	Method C
λ_{max}, nm	520	610	550
Beer's law limits, μg mL^{-1}	0.125–1.75	1.0–10.0	1.0–9.0
Molar absorptivity, L moL^{-1} cm^{-1}	3.94×10^4	1.45×10^4	1.99×10^4
Sandell sensitivity, μg cm^{-2}	0.0057	0.0154	0.0112
Limit of detection, μg mL^{-1}	0.03	0.15	0.11
Limit of quantification, μg mL^{-1}	0.11	0.44	0.34
Regression equation, Y*			
Intercept (a) Slope (b)	0.017	–0.003	0.004
Slope (b)	0.159	0.067	0.085
Correlation coefficient, (r)	0.9987	0.9997	0.9994
S_a	0.00858	0.0055	0.0218
S_b	0.00324	0.0006	0.0024

*Y = a+bX, where Y is the absorbance and X concentration in μg mL^{-1}. S_a = Standard deviation of intercept. S_b = Standard deviation of slope.

drug added was quantitative (97.7-104.2%) and revealed that co-formulated substances such as talc, starch, gelatin, gum acacia, calcium carbonate, calcium gluconate, calcium dihydrogen orthophosphate, sodium alginate and magnesium stearate did not interfere in the determination.

CONCLUSIONS

Four useful micro methods for the determination of STV have been developed and validated as per the current ICH guidelines (ICH guidelines, 1996, 2005). The proposed methods are simple, rapid and cost-effective. The methods are one of the most sensitive ever reported

TABLE III
Intra-day accuracy and precision of the methods.

Method*	STV taken	STV found, **	Range	Relative error, %	SD	SEM	RSD, %	CL
Titrimetry	4.0	3.93	0.14	1.75	0.033	0.013	0.84	3.93 ± 0.031
	6.0	5.85	0.18	2.50	0.134	0.051	2.29	5.85 ± 0.124
	9.0	8.82	0.12	2.00	0.054	0.020	0.61	8.82 ± 0.049
Spectro-photometric method A	0.5	0.49	0.07	1.70	0.005	0.002	0.96	0.49 ± 0.010
	1.0	0.98	0.05	1.48	0.008	0.003	0.85	0.98 ± 0.021
	1.5	1.47	0.07	1.45	0.017	0.006	1.14	1.47 ± 0.025
Spectro-photometric method B	3.0	2.93	0.07	2.33	0.033	0.013	1.13	2.93 ± 0.031
	6.0	5.85	0.05	2.45	0.064	0.024	1.09	5.85 ± 0.059
	9.0	8.89	0.07	1.18	0.076	0.029	0.85	8.89 ± 0.070
Spectro-photometric method C	2.0	1.95	0.07	2.50	0.029	0.011	1.49	1.95 ± 0.027
	4.0	3.89	0.05	2.75	0.036	0.014	0.93	3.89 ± 0.033
	8.0	7.92	0.07	1.03	0.065	0.025	0.82	7.92 ± 0.060

*In titrimetry taken/found/range, SD and SEM are in mg while in spectrophotometric methods the they are in μg mL^{-1}. **Mean value of seven determinations SD = Standard deviation; SEM = Standard mean of error; RSD = Relative standard deviation; and CL = Confidence limits at 95% confidence level for six degrees of freedom.

TABLE IV
Results of assay of STV in dosage forms by proposed methods and statistical comparision with reference method.

Dosage form and brand name*	Nominal amount, mg per tablet/	% Found Ψ ± SD				
		Reference Methods	Titrimetry	Spectrophotometry		
				Method A	Method B	Method C
Capsule						
STAG[a]	30	102.3 ± 0.96	100.9 ± 1.51 t = 1.79 F = 2.47	101.1 ± 1.42 t = 2.31 F = 2.19	100.5 ± 1.51 t = 1.59 F = 2.44	101.3 ± 1.46 t = 1.31 F = 2.31
STAVIR[b]	40	98.54 ± 1.24	99.8 ± 1.79 t = 1.31 F = 2.08	99.7 ± 1.98 t = 1.33 F = 2.55	101.1 ± 1.85 t = 2.62 F = 2.23	100.7 ± 1.95 t = 2.14 F = 2.47
Tablets						
VIROSTAV[c]	30	101.3 ± 0.62	100.9 ± 1.25 t = 0.68 F = 4.06	99.9 ± 1.42 t = 2.17 F = 5.25	102.9 ± 1.21 t = 2.76 F = 3.81	102.4±1.42 t = 1.70 F = 5.25

*Marked by: a = Cross lands; b = Cipla India Ltd; c = Genix Pharm. India. Ψ = Mean value of five determinations. Tabulated value of t at 95% confidence level is 2.77 and tabulated F-value at the same level confidence is 6.39 both for four degrees of freedom.

TABLE V
Results of recovery study via standard-addition method.

Method	Tablet studied	STV in formulation	Pure STV added	Total found	Pure STV recovered*, %
Titrimetry	VIROSTAV 30	3.03	2.0	5.08	102.5
		3.03	4.0	7.08	101.2
		3.03	6.0	8.95	98.6
Spectro-photometric method A		5.00	3.0	8.08	102.5
		5.00	7.0	12.08	101.2
		5.00	9.0	13.87	98.6
Spectro-photometric method B		20.58	20.0	40.52	99.7
		20.58	40.0	59.90	98.3
		20.58	80.0	101.06	100.6
Spectro-photometric method C		10.24	20.0	30.88	103.2
		10.24	40.0	49.52	98.2
		10.24	80.0	90.64	100.5

*Mean value of three determinations. In titrimetry STV in dosage form/pure STV added are in mg. In spectrophotometric methods the same are in μg.

for stavudine and are superior to the existing HPLC and UV-spectrophotometric methods. They rely on the use of simple and cheap chemicals, and inexpensive techniques but provide a sensitivity comparable to that achieved by sophisticated and expensive technique like HPLC. These advantages coupled with good accuracy and precision make the methods highly suitable for routine use in laboratories as a part of industrial quality control.

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RESUMO

Este trabalho descreve quatro métodos rápidos e sensíveis para a determinação de estavudina (STV) na matéria-prima ou em produtos formulados. Soluções aquosas de STV podem ser tituladas tratando-as com excesso de bromato-brometo em meio ácido clorídrico, seguido da determinação iodimétrica de bromo em excesso. Métodos espectrofotométricos também envolvem a adição de excesso de bromato-brometo à amostra, seguida da determinação de bromo residual por adição de uma quantidade fixa de alaranjado de metila, índigo-carmim ou azul de timol, e de medidas de absorbância nos comprimentos de onda apropriados: 520, 610 ou 550 nm. Em todos os métodos, a quantidade de bromato consumida corresponde à quantidade de STV e os resultados da sua aplicação à determinação de STV em comprimidos e cápsulas são satisfatórios.

Palavras-chave: determinação de estavudina, titulometria, espectrofotometria, bromato-brometo, corantes, fármacos.

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