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Validated method for Vinblastin by Spectrophotometry in Bulk Drug and Pharmaceutical formulations

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ABSTRACT

A simple, rapid and sensitive spectrophotometric method for the determination of vinblastine in pure form and in pharmaceutical. Formulations is described .The method is based on the simple solubility of vinblastine in methanol. The absorbance maximum of vinblastine measured at wave length 420 nm. The drug obeys Beer's Law in the concentration range 6-16 µg/ml employed for this method. Accuracy and reproducibility of the proposed method was statistically validated by recovery studies. The method is found to be rapid, precise and accurate and can easily be employed in the laboratory for the routine estimation of drug and it's extended to the analysis of vinblastine in pharmaceutical formulations.

Key words: vinblastine, Validation parameters, Spectrophotometric Estimation, UV-Visible spectrophotometer

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INTRODUCTION

Vinblastine is an antimicrotubule drug used to treat certain kinds of cancer, including Hodgkin's lymphoma, non-small cell lung cancer, breast cancer, head and neck cancer, and testicular cancer. It is also used to treat Langerhans cell histiocytosis. Vinblastine was traditionally obtained from Catharanthus roseus, also known as Vinca rosea, a Madagascar Periwinkle. It is generated in the plant by the joining of two alkaloids catharanthine and vindoline.[1]

Vinblastine was first isolated by Robert Noble and Charles Thomas Beer at the University of Western Ontario from the Madagascar periwinkle plant. Vinblastine's utility as a chemotherapeutic agent was first suggested by its effect on the body when the plant was consumed in a tea. Drinking the tea led to a decreased number of white blood cells, so it was hypothesized that vinblastine might be effective against cancers of the white blood cells such as lymphoma.Vinblastine is a vinca alkaloid and a chemical analogue of vincristine. It binds tubulin, thereby inhibiting the assembly of microtubules. It is M phase cell cycle specific since microtubules are a component of the mitotic spindle and the kinetochore which are necessary for the separation of chromosomes during anaphase of mitosis. Toxicities include bone marrow suppression (which is dose-limiting), gastrointestinal toxicity, potent vesicant (blister-forming) activity, and extravasation injury (forms deep ulcers). Vinblastine paracrystals may be composed of tightly-packed unpolymerized tubulin or microtubules.[2]

Vinblastine is reported to be an effective component of certain chemotherapy regimens, particularly when used with bleomycin, and methotrexate in VBM chemotherapy for Stage IA or IIA Hodgkin lymphomas. The inclusion of vinblastine allows for lower dosese of bleomycin and reduced overall toxicity with larger resting periods between chemotherapy cycles.[3]Microtubule disruptive drugs like vinblastine, colcemid, nocodazole have been reported to act by two mechanisms.[4] At very low concentrations they suppress microtubule dynamics and at higher concentrations they reduce microtubule polymer mass. Recent findings indicate that they also produce microtubule fragments by stimulating microtubule minus-end detachment from their organizing centers. Dose-response studies further indicate that enhanced microtubule detachment from spindle poles correlate best with cytotoxicity.[5]

Vinblastine may be isolated from the Madagascar Periwinkle (Catharanthus roseus), along with several of its precursors- catharanthine and vindoline. Extraction is costly and yields of vinblastine and its precursors are low. Enantioselective synthesis has been of considerable interest in recent years, as the natural mixture of isomers is not an economical source for the required C16'S, C14'R stereochemistry of biologically active vinblastine. Initially, the approach depends upon an enantioselective Sharpless epoxidation, which sets the stereochemistry at C20. The desired configuration around C16 and C14 can then be fixed during the ensuing steps. In this pathway, vinblastine is constructed by a series of cyclization and coupling reactions which create the required stereochemistry. The overall yield may be as great as 22%, which makes this synthetic approach more attractive than extraction from natural sources, whose overall yield is about 10%.[6] Stereochemistry is controlled through a mixture of chiral agents (Sharpless catalysts), and reaction conditions (temperature, and selected enantiopure starting materials).[7]

The antineoplastic drugs widely used in the treatmentof Hodgkin's disease, lymphocytic lymphoma, advancedbreast cancer, advanced testicular cancer, acute leukemia,and Kaposi's sarcoma (8–10).A varietyof methods proposed for their determination include s radioimmunoassay (11–13), liquid chromatographic methods(14–19), thin-layer chromatography (20–21), voltammetric methods (22–25), polarography (26), and UVspectrophotometry (27). VBS and VCS are official in the British,Indian, and U.S. Pharmacopeias (28–30). Therefore, an attempt was made to develop a simple spectrophotometric method for the estimation of the present drug in bulk and pharmaceutical formulations

EXPERIMENTAL SECTION

Methanol and chloroform were of AR grade. GEMZAR tablet (vinkem labs limited Chennai tamilnadu), VELBAN capsule (serum international) were purchased from the market. Simandzu uv-1700 & 1800 uv/vis spectrophotometers with 10 mm matched quartz cells was used for experiment. Absorption and overlain spectra were recorded over the wavelength range of 200-500 nm, using 1cm quartz cells at a scan speed medium and fixed slit width of 1.0 nm

Preparation of standard stock solution:
Standard vinblastin 100mg was dissolved in 100ml methanol to make 1000µg/ml stock solution.

Procedure for the Determination of vinblastin standard:
From the above solution aliquots of 0.6 ml, 0.8 ml, 1 ml, 1.2 ml, 1.4 ml, 1.6 ml were taken in a separate 10 ml volumetric flasks then make up the volume with methanol.

Procedure for the Determination of vinblastin in Drug Formulations:
An amount of the powdered tablet and capsule equivalent to 100 mg of vinblastin was weighed accurately, and extracted into 3 × 20 ml portions of chloroform with shaking. The residue was filtered using Whatmann No. 42 filter paper. The filtrate was evaporated to dryness under vacuum and the remaining drug was dissolved in methanol and diluted to 100 ml.

RESULTS AND DISCUSSION

Absorption maxima of vinblastin were detected at 420 nm . Absorbance at different concentration showed in (Table 1). Linearity graph was showed in (Figure 2). Optical characteristics data showed in (Table 2), Repeatability data for analysis of vinblastin in(Table 3). Reproducibility data for analysis of vinblastin were in (Table 4). The absorptivity coefficient of drug was determined by using equation A=abc. Recovery studies were done so as to check the accuracy of the method which was mentioned in (Table 5). Results of analysis of vinblastin in marketed formulation were showed in (Table 6).

Table 2 : Calibration data for analysis of vinblastin at 420nm

Concentration (µg/ml)	Absorbance Mean ± S.D.
6	0.247±0.003
8	0.326±0.002
10	0.398±0.002
12	0.483±0.001
14	0.559±0.001
16	0.634±0.001

Figure 1: Structure of VINBLASTIN

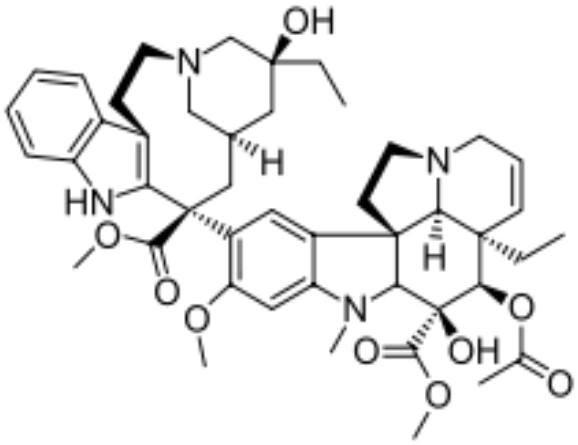

Figure 2: Results of linearity graph of VINBLASTIN

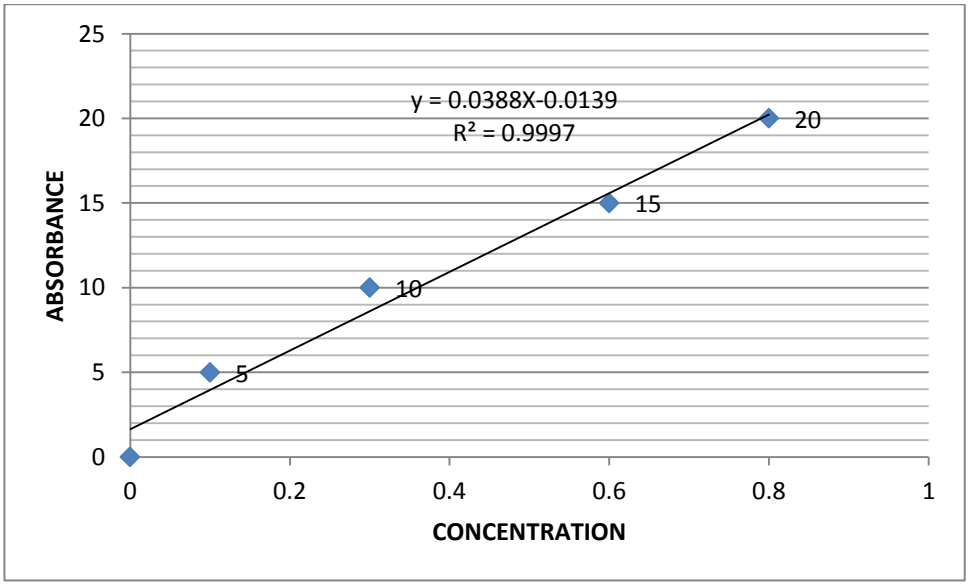

Table 4 : Optical characteristics OF VINBLASTIN

parameters	Value
λmax (nm)	420
Beer's law limit (µg/ml)	6-16
$A1^{\%}1cm$	402.53
Correlation coefficient (r2)	0.9997
Regression Equation (y=a+bc)	Y=0.0388x-0.0139
Intercept (a)	0.0139
Slope (c)	0.0338
Limit of quantification (µg/ml)	0.9
Limit of detection (µg/ml)	0.29

Table 5 : Repeatability data for analysis of vinblastine

Concentration (µg/ml)	Intraday	Interday
	Absorbance (Mean ± S.D.)	Absorbance (Mean ± S.D.)
8	0.325 ± 0.0037	0.327 ± 0.0031
12	0.485 ± 0.0053	0.483 ± 0.0049
16	0.636 ± 0.0048	0.639 ± 0.0053

Table 6 : Reproducibility data for analysis of vinblastine

Concentration (µg/ml)	Absorbance	
	UV 1700 (Mean ± S.D.)	UV 1800 (Mean ± S.D.)
8	0.324±0.002	0.325±0.003
12	0.486±0.002	0.490±0.002
16	0.634±0.003	0.638±0.003

Table 5: Accuracy data for analysis of vinblastine (Recovery studies)

Amount of sample taken (µg/ml) (A)	Amount of standard added (µg/ml) (B)	Total Amount (A + B) (µg/ml)	Total amount found (µg/ml)	% Recovery
10	**8**	**18**	**17.825**	**99.03**
10	**10**	**20**	**20.337**	**101.69**
10	**12**	**22**	**22.129**	**100.59**

Table 6: Analysis of marketed formulations

Formulation	%Amount Found ± SD
GEMZAR	**99.84±0.0039**
VELBAN	**101.97±0.0031**

CONCLUSION

The developed method is useful due to high tolerance limit for common Excipients found indrug formulations. The developed method does not require any elaborate treatment of the drug and tedious extraction procedure for the formation of colored chromophore of the drug with the interacting reagents also. The method which we developed for the validation was studied at 420 nm wave length. Accuracy and reproducibility was determined by calculating the recovery study that was close to 100%. The developed method is simple, precise, accurate and reproducible. Due to high sensitivity and simple sample preparation, the method can be used for routine analysis.

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