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SPECTROPHOTOMETRIC ESTIMATION OF GRANISETRON IN BULK AND TABLET FORMULATION

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ABSTRACT

Three simple, precise and economical spectrophotometric methods have been developed for the estimation of granisetron in bulk and pharmaceutical preparations. Method A involves the determination of granisetron by dissolving in distilled water and followed by measuring the absorbance at 301 nm. Method B involves the derivatisation of the primary spectra to the second order. The drug obeyed Beer's law in the concentration range of 5-50 μg/mL for both the methods. Method C is based on the reaction of granisetron with ferric chloride and 1,10-phenanthroline to form blood red coloured chromogen and followed by measuring the absorbance at 510 nm. The results of the analysis were validated statistically and found to be satisfactory.

Key words: Granisetron (GSN), Spectrophotometry, Beer's law, Derivative spectrophotometry, Visible spectrophotometry.

INTRODUCTION

Granisetron is chemically 1-methyl–N–(1R, 3R, 5S)–9–methyl–9–azabicyclo(3,3,1) nonan 3–yl–1H imidazole–3–carboxamide and is used as an antiemetic in chemotherapy induced vomiting. No method of estimation for granisetron (GSN) in bulk and formulation has been reported so far; except RP–HPLC method of estimation of the drug in biological fluids[1-3].

EXPERIMENTAL

Instrumentation

All spectral measurements were made on Shimadzu UV-VIS spectrophotometer–

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1650 with 1 cm matched quartz cells.

Preparation of standard stock solution

An accurately weighed amount of 100 mg of GSN taken in 100 mL volumetric flask and dissolved in 25 mL of distilled water and then made up to volume with distilled water.

Preparation of sample solution

The average weight of 20 tablets of GSN was determined and finely powdered. The powder equivalent to 10 mg of GSN was taken in 100 mL volumetric flask and dissolved in 25 mL of distilled water and then made up to volume with the same distilled water. The solution was then filtered, the first few mL of the filtrate was discarded and remaining solution was used for the analysis.

Reagents

All the reagents used were of analytical reagent grade. All the solutions were freshly prepared with distilled water. The reagents used in method C were ferric chloride (0.03M) and 1,10-phenanthroline (0.01M).

Assay procedure

Method A

Aliquots of the standard stock solution were transferred to a series of 100 mL volumetric flask and suitably diluted to give a varying concentrations ranging from 5–50 µg/mL and the solutions were scanned in the spectrum mode from 400-200 nm using distilled water as blank. It was found that GSN exhibits an absorbance maximum at about 301 nm. A calibration graph was obtained by plotting concentration versus absorbance. It obeyed Beer's law[4] in the range of 5-50 µg/mL. The sample solution was suitably diluted to get a concentration between 5–50 µg/mL and the procedure adopted for standard solutions was followed. The absorbance obtained for the sample was then interpolated on the calibration graph and the concentration of GSN in the sample was then determined.

Method B

Aliquots of the standard stock solution were transferred to a series of 100 mL volumetric flask and suitably diluted to give a varying concentrations ranging from 5–50 µg/mL and the solutions were scanned in the spectrum mode from 400-200 nm using distilled water as blank. The normal spectrum obtained was derivatized to the second order[4]

using derivative mode. The amplitude (DL) of long wave peak satellite of the second order curve was measured in mm. The amplitudes of the derivative spectra at 301 nm were noted. A calibration graph was obtained by plotting concentration versus amplitude. The sample solution was suitably diluted to get a concentration between 5–50 µg/mL and the procedure adopted for standard solutions was followed. The amplitude obtained for the sample was then interpolated on the calibration graph and the concentration of GSN in the sample was then determined.

Method C

In to a series of 25 mL standard flask, 0.5-3.0 ml (1 mL = 200 µg/mL) of working standared solution was pipetted separately and 1 mL of 0.03 M ferric chloride solution and 1.5 mL of 0.01M 1,10-phenanthroline[5] was added. The standard flask were then heated on a water bath for 15 minutes at 60° C, cooled to room temperature and the total volume was made upto 25 mL with distilled water. The absorbance of the blood red coloured species was measured at 510 nm against reagent blank. The amount of granisetron present in the sample solution was computed from its calibration curve.

RESULTS AND DISCUSSION

The optical characteristics such as RSD, regression equation, correlation coefficient, slope and intercept for the three methods were calculated and the results are summarized in Table 1. To evaluate the validity and reproducibility of the methods, recovery studies were carried out by adding a known amount of pure drug to previously analyzed tablet powder sample and re-analyzed. The results obtained are presented in Table 2. Interference studies revealed that the excipients and additives did not interfere. Hence, these methods are most economic, simple, sensitive and accurate and can be used for the routine determination of GSN in pharmaceutical preparations.

Table 1: Optical characteristics for granisetron

Parameters	Method A	Method B	Method C
λmax (nm)	301	301	510
Beer's law limit (µg/mL)	5-50	5-50	4-24

Cont...

Parameters	Method A	Method B	Method C
Molar absorptivity (L mol^{-1} cm^{-1})	$1.00743x10^4$	-	$1.90805x10^4$
Sandell's sensitivity (µg cm^{-2}/ 0.001 abs unit)	0.031012	-	0.001833
Slope	0.032041	1.440	0.051026
Intercept	0.0039	0.13636	0.027964
Regression equation (y = mx + c)	0.032041x + 0.0039	1.440x + 0.13636	0.051026x + 0.027964
Corelation coefficient	0.9999	0.9994	0.9998
% RSD	0.2693	0.4593	0.3228
LOD	0.84352	0.65213	3.91842
LOQ	2.556122	4.59644	11.874

Table 2: Assay and recovery of granisetron and its formulations

Method	Drug	Label Claim (mg/tablet)	Amount obtained (mg)*	% Label claim	**% Recovery by the proposed methods*
Method A	GSN	1.000 mg	1.0109	101.09	100.2
Method B			1.0211	102.11	99.8
Method C			1.0147	101.47	101

* Each average of three determinations, GSN-Granisetron

** After spiking the sample

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