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Development Of Simple And Sensitive Visible Spectrophotometric Methods For The Determination Of Granisetron Hydrochloride In Pure And Pharmaceutical Formulations

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Abstract: Two simple, sensitive, and accurate spectrophotometric methods were developed for the estimation of Granisetron HCl in bulk and dosage forms. Method A is based on the formation of charge transfer complex between the drug and chloranilicacid (CA) in presence of methanol, the colored product was quantified at a maximum wavelength 518 nm. Whereas method B is based on the reduction of Folin Ciocalteau (FC) reagent in alkaline medium by Granisetron HCl leading to the formation of intense blue colored chromogen shows the λ_{max} at 760nm. The optical characteristics (such as Beers law limits, molar absorptivity and Sandell's sensitivity) and regression parameters (such as slope (b), intercept (a) and correlation coefficient (r) and standard error of estimation (Se)) for the two methods were determined. The molar absorptivity of the two reactions was found to be 7.656 and 9.625 $lt.mol^{-1}.cm^{-1}$ respectively**.** Determinations of Granisetron HCl in bulk form and in pharmaceutical formulations were also incorporated.
Key words: Granisetron HCl**,** Chloranilic acid**,** F.C.reagent, Optical characteristics and Regression parameters.

INTRODUCTION

The Granisetron hydrochloride salt is a white to off-white crystalline powder; soluble in water and saline; administered intravenously. Chemical designation is endo-N-(9-methyl-9- azabicyclo [3.3.1] non-3-yl)-1-methyl-1H- indazole-3-carboxamide hydrochloride. The molecular formula and its gram molecular weight are $C_{18}H_{24}N_4O\cdot HCl$ and 348.87grams/mole respectively. It is an antiemetic agent to prevent the nausea and vomiting in conjunction with cancer chemotherapy or with radiation therapy, by blocking 5-HT_3 receptors without having effect on other receptors such as dopamine D_2 receptor and 5-HT_4 receptor. It works by blocking serotonin, a natural substance in the body that causes nausea and vomiting due to the anaesthetics[1, 2]. Granisetron dosage forms are not yet official in USP[3] and BP[4]. An extensive literature survey is carried out and found that some HPLC[5-12] methods have been reported for the determination of Granisetron HCl mostly in plasma and a few in pharmaceutical formulations and an UV spectrophotometric method[13] in dosage forms. The main objective of the present work is to develop a simple, precise and accurate spectrophotometric method for the estimation of Granisetron HCl in pharmaceutical dosage forms. The chemical structure of the Granisetron is presented in Fig.1.

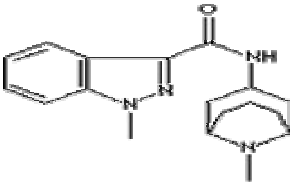

Fig.1 Chemical structure of Granisetron

EXPERIMENTAL

Materials and Methods

All the spectral measurements were made on ELICO SL-207 double beam UV-Visible spectrophotometer. All the chemicals (chloranilic acid, acetonitrile, methanol and sodium carbonate) were of analytical grade were used. Distilled water was used to prepare all the solutions and in all experiments. CA Solution (0.1%, Loba) was prepared by dissolving 100 mg of p-chloranilicacid in 20 ml of iso propyl alcohol and diluted to 100 ml with chloroform. Sodium carbonate (Na_2CO_3) solution (10%, $9.43x10^{-1}$ M): Prepared by dissolving 10 gm sodium carbonate in 100 ml distilled water. Folin Ciocalteau reagent (FC) (Loba, 2N) was used as it is. About 100mg of Granisetron HCl was accurately weighed, transferred to a standard 100 ml volumetric flask and dissolved in 20 ml of distilled water and. The final volume was made up to the mark with distilled water. Further 25 ml of the stock solution was diluted to100ml with distilled water obtain the final concentration 250µg/ml. Twenty tablets were weighed accurately and reduced to fine powder, drug equivalent to 10mg of Granisetron HCl and 5-7ml of methanol were taken in a 10ml volumetric flask, sonicated for about 5 min, and the volume was made up to 10ml with distilled water and filtered by using Whattmann filter paper. The filtrate was quantitatively diluted with water to yield concentrations in the linear range of the assay of Granisetron HCl.

Recommended procedures for the determination of Granisetron HCl

Method A

Into a series of 25.0ml calibrated tubes containing aliquots of standard Granisetron solution (0.5ml-2.5ml,250µg/ml), 2.0ml of p-chloranilic acid(0.1%) was added and kept aside for 30 min at lab temperature. The volume in each tube was made up to the mark with alcohol. The absorbance of the colored species was measured at 518nm against a reagent blank.

Method B

Delivered different aliquots of standard drug solution (0.5-2.5ml, 250µg/ml) into a series of 25.0ml calibrated tubes and the volume were adjusted to 3.0ml with distilled water. To each of test tubes 5.0ml of Na_2CO_3 and 1.5ml of F.C reagent were added and kept aside for 5min. The volume was brought to the mark with distilled water. The absorbance was measured after 15min at 760nm against a reagent blank prepared under identical conditions.

RESULTS AND DISCUSSION

Beer's law was obeyed over the concentration range of 5-25 µg/.ml for method A and method B. The proposed procedures are validated by determining various optical parameters, which are listed in Table 1.The linearity, intercepts and the slope have been calculated using regression equation Y= a+bC, where Y represents optical density, C is the concentration of the drug in µg /mL and 'a' and 'b' represents intercepts and slope respectively. Precision and accuracy of the proposed methods were tested by carrying out the determination of six replicates of pure and dosage samples of the drug, whose concentration lie within Beer's law range. The values of standard deviation (% R.S.D.) and percent range of error (0.05 level and 0.01 level confidence limits) were calculated for the above two methods are presented in Table-1. The values obtained for the determination of Granisetron HCl in different brands of tablet by the proposed and U.V reference methods are compared in Table-2 Table-3. Both the methods proposed carried at room temperature for the formation of colored species. The absorption spectra of the two methods show that the maximum wavelength (λ_{max}) was determined which have been represented in Fig.2 and Fig.3. Calibration curves for the two methods were prepared Fig.4 and Fig.5 by plotting the absorbance versus the concentration. In method A, the drug GSH formed immediate purple color with chloranilic acid (CA) due to formation of a charge transfer complex (CT). The CT complex formation is evidenced by the absorption wave length of CA at 430nm is shifted to 518 nm in the presence of drug GSH. CA is a well known π acceptor and drug is n-donor.CA has been used for the spectrophotometric determination of drugs containing n-electron donors such as nitrogen and oxygen. In this reaction the CT complex is formed by the donation of electrons from the tertiary nitrogen moiety present in the drug. In method B, the reduction of Folin-Ciocalteau reagent(FC) i.e.

hetropoly acid, phospho-molybdotungstic acid, by the Granisetran HCl in the presence of alkali thereby producing one or more possible reduced species which have a characteristic intense bluish-green colored chromogen with λ max at 760 nm.

Table 1: Optical and regression characteristics, precision and accuracy of the proposed methods

Optical characteristics	Method A	Method B
λ_{max} (nm)	518	760
Beer's law limits (µg/mL)	5.0-25.0	5.0 - 25.0
Molar absorptivity (1 $mol^{-1}.cm^{-1}$)	$7.656x10^3$	9.625×10^3
Sandell's sensitivity (µg.cm^{-2}/0.001 absorbance Unit)	0.0408	0.03246
Optimum photometric range (µg/mL)	6.5-17.5	5.0 – 20.0
Regression equation (Y=a+bc) ;Slope (b)	0.0240	0.030
Standard deviation on slope (S_b)	$1.95x10^{-4}$	$8.9x10^{-4}$
Intercept (a)	0.0019	0.003
Standard deviation on intercept (S_a)	$3.24x10^{-3}$	$1.48x10^{-3}$
Standard error on estimation (S_e)	0.00309	0.00144
Correlation coefficient (r)	0.9998	0.9999
Relative standard deviation (%)	1.0322	0.5104
0.05 level	0.8632	0.4268
0.01 level	1.2769	0.6314
LOD	0.4456	0.1631
LOQ	1.3505	0.4944

*** Average of six determinations considered**

Table: 2 Estimation of Granisetron HCl in pharmaceutical dosage forms.[Method –A]

Name of the dosage form	Label amount claimed (mg/tablet)	Amount of the drug found(mg)**	Standard deviation	% Recovery
Tablet-1	5.0	4.96	0.0779	99.20
Tablet-2	10.0	9.85	0.0593	98.50

Table: 3 Estimation of Granisetron HCl in pharmaceutical dosage forms.[Method –B]

Name of the dosage form	Label amount claimed(mg/tablet)	Amount of the drug found(mg)**	Standard deviation	% Recovery
Tablet-1	5.0	5.03	0.0689	100.6
Tablet-2	10.0	9.98	0.0745	99.80

****Average of six determinations considered**

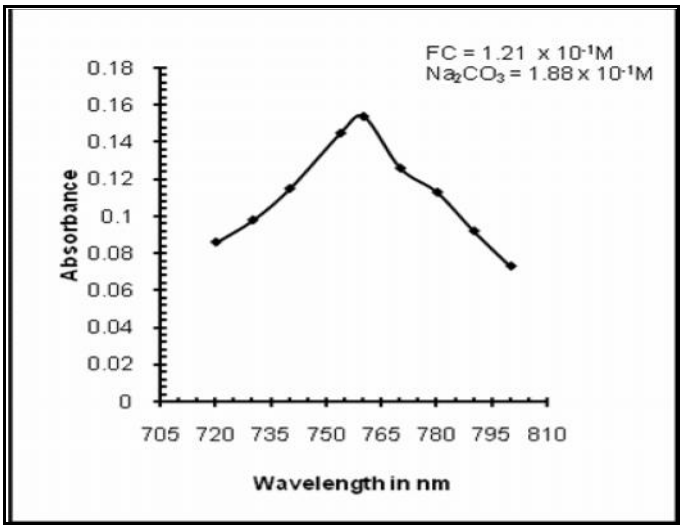

Fig-2 Absorption spectra for reaction between Granisetron HCl and chloranilicacid (CA) in presence of methanol (Method-A)

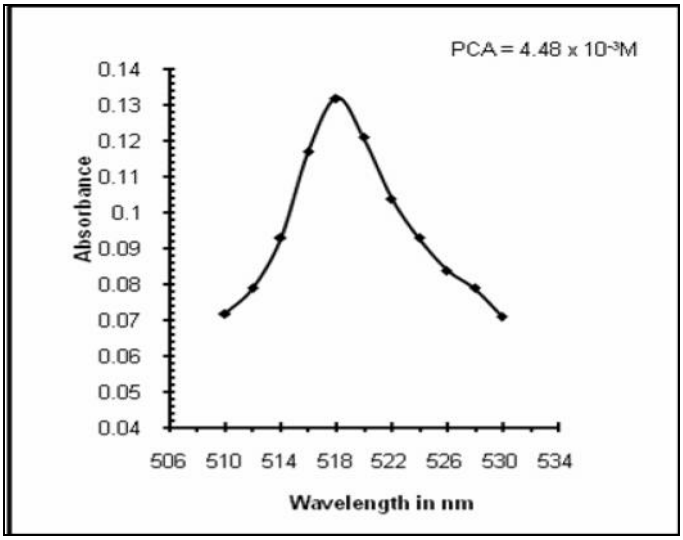

Fig-3 Absorption spectra for the reduction of Folin Ciocalteau (FC) in alkaline medium by Granisetron HCl (Method-B

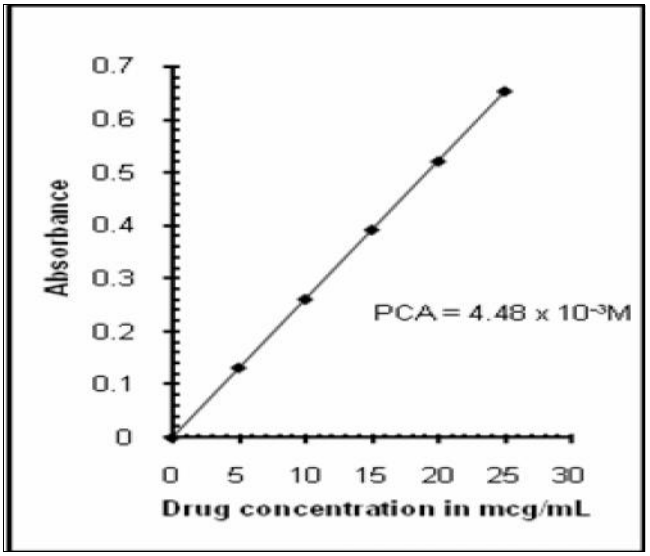

Fig-4 Calibration plot for reaction between Granisetron HCl and chloranilicacid (CA) in presence of methanol (Method-A)

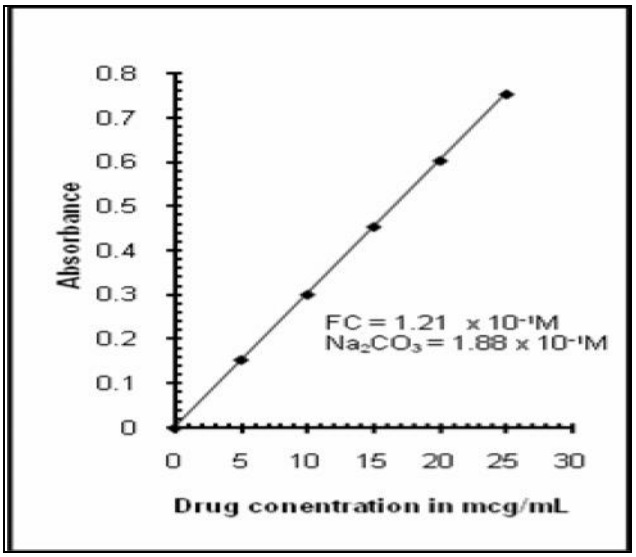

Fig-5 Linearity plot for the reduction of Folin Ciocalteau (FC) in alkaline medium by Granisetron HCl (Method-B)

CONCLUSIONS

The methods reported here are found to be simple, sensitive, accurate and precise. Further, spectrophotometric methods involve simple instrumentation which is cost effective compared with other instrumental techniques, which ordinary laboratories cannot afford to have. The present methods involve the formation of highly stable colored species which makes it easier for the determination of Granisetron HCl in pharmaceutical dosage forms.

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