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Research Article

DETERMINATION OF GANCICLOVIR IN BULK AND PHARMACEUTICAL DOSAGE FORMS BY UV SPECTROPHOTOMETRIC METHOD

C.M. Bhaskar Reddy[1]*, G.V. Subba Reddy[2]

[1]Research Scholar, Rayalaseema University, Kurnool - 518002 A. P., India

[2]Associate Professor of Chemistry, Dept of Chemistry, JNTU College of Engineering, Pulivendula, Kadapa (DT) A. P., India

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*E-mail: cmbr2008@gmail.com

ABSTRACT:

A Simple, rapid, accurate and economical UV Spectrophotometric method is developed for determination of Ganciclovir in bulk and tablets. In chloroform, the λmax of the drug was found to be 240 nm. Using double-beam Analytical Technologies Limited, model T60 UV-Visible spectrophotometer connected to computer loaded with UV Win 5.0 software, in this proposed method Ganciclovir follows linearity in the concentration range 1 – 40µg/ml with a correlation coefficient of 0.998. Assay results were in good agreement with label claim. The methods were validated statistically and by recovery studies. The relative standard deviation was found to be 0.2319 with excellent precision and accuracy. The proposed method is specific while estimating the commercial formulations without interference of excipients and other additives. Hence, this method can be used for the routing determination of Ganciclovir in bulk samples and pharmaceutical formulations

Key words: Ganciclovir, UV Spectrophotometry, Chloroform.

INTRODUCTION

Ganciclovir is chemically 2-amino-1,9-[{2-hydroxy-1-(hydroxymethyl) ethoxy} methyl]-6- H-purine-6-H-one[1-4]. Ganciclovir is an antiviral medication used to treat or prevent cytomegalovirus (CMV) infections.Ganciclovir sodium is marketed under the trade names Cytovene and Cymevene (Roche). Ganciclovir for ocular use is marketed under the trade name Vitrasert (Bausch & Lomb). A prodrug form with improved oral bioavailability (valganciclovir) has also been developed.[5] Ganciclovir is a synthetic analogue of 2'-deoxy-guanosine. It is first phosphorylated to a deoxyguanosine triphosphate (dGTP) analogue. This competitively inhibits the incorporation of dGTP by viral DNA polymerase, resulting in the termination of elongation of viral DNA[5]. Absorption of the oral form is very limited - about 5% fasting, about 8% with food. It achieves a concentration in the central nervous system of about 50% of the plasma level. About 90% of plasma ganciclovir is eliminated unchanged in the urine, with a half-life of 2-6 hrs, depending on renal function (elimination takes over 24 hours in end-stage renal disease).[5] Ganciclovir is indicated for6 sight-threatening CMV retinitis in severely immuno compromised people. CMV pneumonitis in bone marrow transplant recipients Prevention of CMV disease in bone marrow and solid organ transplant recipients Confirmed CMV retinitis in people with AIDS (intravitreal implant)[6]. It is also used for acute CMV colitis in HIV/AIDS and CMV pneumonitis in immune suppressed patients. Ganciclovir has also been used with some success in treating human herpesvirus-6 infections[7]. Ganciclovir is commonly associated with a range of serious haematological adverse effects. Common adverse drug eactions (≥1% of patients) include: granulocytopenia, neutropenia, anaemia, thrombocytopenia, fever, nausea, vomiting, dyspepsia, diarrhoea, abdominal pain, flatulence, anorexia, raised liver enzymes, headache, confusion, hallucination, seizures, pain and phlebitis at injection site (due to high pH), sweating, rash, itch, increased serum creatinine and blood urea concentrations[6]. Ganciclovir is considered a potential human carcinogen, teratogen, and mutagen. It is also considered likely to cause inhibition of spermatogenesis. Thus, it is used judiciously and handled as a cytotoxic drug in the clinical setting[6,8] it is a synthetic nucleoside analogue closely related to Acyclovir It is used in the treatment of cytomegalovirus (CMV) infection in AIDS patients. GCV exhibits antiviral activity against herpes simplex virus (HSV) and cytomegalovirus (CMV) at relatively low inhibitory concentrations. It is official in Martindale, Merck Index, USP. Literature survey reveals that few High performance liquid chromatographic (HPLC) methods have been described for analysis of GCV in serum and human plasma. Those methods include ion-pairing agents[9,10], gradient elution[11], amperometric detection[12], precolumn flurosecence derivatization[13], electrochemical detection and ion exchange chromatography[14]. These methods are too expensive and time consuming. The present work describes a simple, economical, accurate and reproducible spectrophotometric method for estimation of Ganciclovir in pharmaceutical formulations The proposed method was successfully applied for determination of Ganciclovir in its pharmaceutical formulations.

METHODS AND MATERIALS

Instruments

A double-beam Analytical Technologies Limited, model T60 UV-Visible spectrophotometer connected to computer loaded with UV Win 5.0 software. The instrument has an automatic Wavelength accuracy of 1 nm and matched quartz cells of 10 mm path length.

Chemicals and Reagents

Ganciclovir, Chloroform (A.R.GRADE), Tablet formulation Natclovir tablets (Natco Pharma Hyderabad, A.P, India)

PREPARATION OF STANDARD STOCK SOLUTION AND STUDY OF CALIBRATION CURVES

The standard stock solution was prepared by dissolving Ganciclovir in chloroform to make final concentration of 100 µg/ml. Different aliquots were taken from stock solution and diluted with chloroform separately to prepare series of concentrations from 1- 40 µg/ml. The λ max was found by UV spectrum of Ganciclovir in chloroform, in the range of 200-400 nm and it was found to be 240 nm. Absorbance was measured at 240 nm against chloroform as blank. The calibration curve was prepared by plotting

absorbance versus concentration of Ganciclovir. The calibration curve was shown in fig-2

Preparation of sample solution

20 tablets of marketed formulation containing Ganciclovir were taken and powdered. The powder equivalent to 10 mg of Ganciclovir was dissolved in 50 ml of chloroform, sonicated for 10 mins and filtered, and total volume is adjusted to 100ml with chloroform. . Different aliquots were taken from sample stock solution and diluted with chloroform separately to prepare series of concentrations from 1-40 µg/ml. nm and it was. The prepared solutions were measured at 240 nm against chloroform as blank. Then the amount of drug present in the formulations was calculated .The results were shown in Table-1

METHOD VALIDATION

Precision

The precision of the proposed method was ascertained by actual determination of eight replicates of fixed amount of the drug. Results given below in Table-3.

Recovery studies

The recovery studies were carried out at three different levels i.e. 80%, 100% and 120% level. To ensure the reliability of the above method, recovery studies were carried out by mixing a known quantity of standard drug with the pre analysed sample formulation and the contents were reanalyzed by the proposed method. The percentage recovery was found and shown in Table-4.

RESULTS AND DISCUSSION

From the optical characteristics of the proposed method it was found that the drug obeys linearity within the concentration range of 1-40 mg/ml. From the results it was found that the percent RSD is less than 2% which indicates that the method has good reproducibility, the percent recovery values of pure drug from the preanalysed solutions of formulations were in between 99.81 -99.8%, which indicates that the method is accurate and which reveals the commonly used excipients and additives present in the pharmaceutical formulations did not interfere in the proposed method. The proposed method was simple, sensitive and reliable with good precision and accuracy. The proposed method is specific while estimating the commercial formulations without interference of excipients and other additives. Hence, this method can be used for the routing determination of Ganciclovir in bulk samples and pharmaceutical formulations.

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TABLE-1 : RESULTS OF ASSAY

Drug	Sample No	Amount Labelled (mg/tab)	Amount Estimated (mg/tab)	% of label Claim	% of Deviation
Ganciclovir	1	60	59.64	99.4	0.6
	2	60	59.66	99.43	0.57
	3	60	59.66	99.43	0.57

TABLE-2 : OPTICAL CHARACTERISTICS OF GANCICLOVIR

parameters	values
Absorption Maximum	240
Linearity Range (mg/ml)	1 - 40
Slope	0.0613
Correlation Coefficient (r)	0.999
% RSD of slope	6.76
Label claim (mg/tablet)	60
Amount found	59.65
S.D	0.0115
RSD%	0.01935
% Recovery	99.01

TABLE-3 PRECISION (GANCICLOVIR)

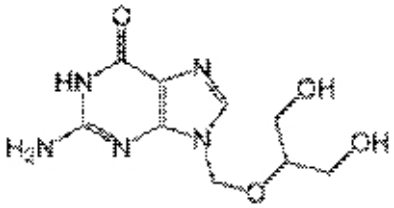
S.N.	Concentration (µg/ml)	Absorbance	Average	S D	%RSD
1	20	1.228	1.228	0.000756	0.0615
2	20	1.230			
3	20	1.229			
4	20	1.228			
5	20	1.229			
6	20	11.228			
7	20	1.228			
8	20	1.228			

The proposed method shows the precision with SD 0.00075 and % RSD 0.0615

Table -4 RECOVERY STUDIES OF GANCICLOVIR

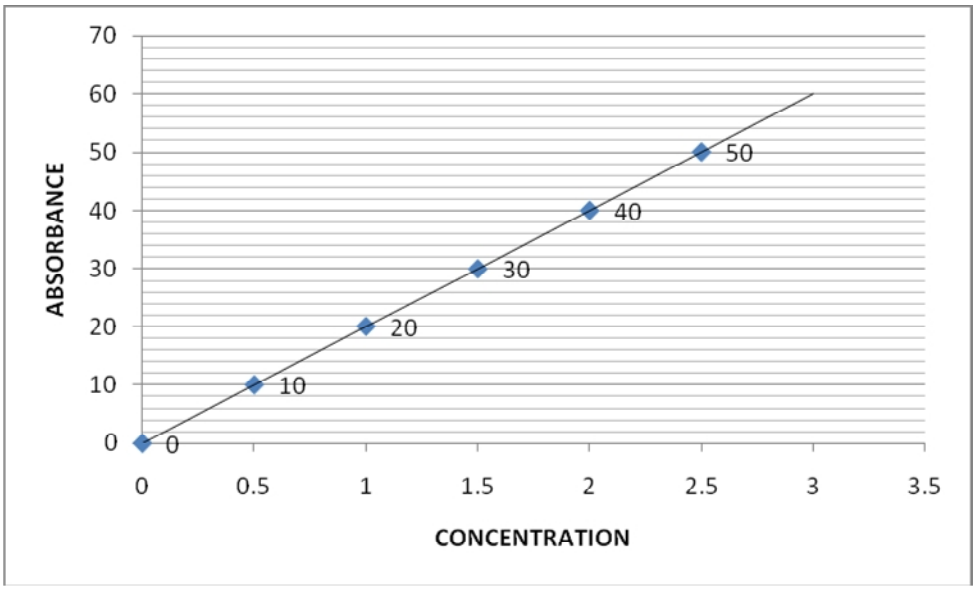
Drug	Amount Added (mg/ml	Amount recovered (mg/ml	Percentage recovery (%)	Average Recovery	%RSD
GANCICLOVER	16	15.97	99.81	99.01	1.2276
	20	19.92	99.6		
	24	23.96	99.8		

FIG: 1 THE STRUCTUREOF GANCICLOVIR



Systematic (IUPAC) name of Ganciclovir
2-amino-9-{[(1,3-dihydroxypropan-2-yl)oxy]methyl}-6,9-dihydro-3*H*-purin-6-one

Figure -2 STANDARD GRAPH OF GANCICLOVER BY UV SPECTROPHOTOMETRIC METHOD



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