CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://zenodo.org/records/10846406

https://www.iajps.com/volumes/volume11-february-2024/59-issue-02-february-24/

Available online at: http://www.iajps.com Review Article

ANALYTICAL METHODS FOR THE DETERMINATION OF GANCICLOVIR IN PHARMACEUTICALS: A MINI REVIEW

Swathi Naraparaju*

Department of Pharmaceutical Chemistry, Gokaraju Rangaraju College of Pharmacy, Hyderabad-500 090, India

Abstract:

Ganciclovir is a purine analogue used in the treatment of cytomegalovirus diseases. The literature survey on ganciclovir revealed a number of analytical methods for its quantification. Present review is focused on method conditions, linearity offered, sensitivity, accuracy, precision and assay results of various analytical methods.

Keywords: *Ganciclovir, Cytomegalo virus, Linearity, Spectroscopic method.*

Corresponding author:

Dr. N. Swathi,

Associate Professor,
Department of pharmaceutical Chemistry,
Gokaraju Rangaraju College of Pharmacy,
Hyderabad-500090,
Telanagana, India.
Mail: swathi8006@grcp.ac.in, swa.pharma@gmail.com
Phone: 9849059163

QR CODE

Please cite this article in press ***N. Swathi****.,* **Analytical Methods For The Determination Of Ganciclovir In Pharmaceuticals: A Mini Review,,** *Indo Am. J. P. Sci, 2024; 11 (02).*

1. INTRODUCTION:

Ganciclovir is an antiviral agent used for the prevention of cytomegalovirus disease in bone marrow and solid organ transplant recipients and also used to treat people with weakened immune system [1] It is chemically known as 2-amino-9-(1,3-dihydroxypropan-2-yloxymethyl)-1H-purin-6-one [2]. The structure of Ganciclovir was shown in Fig. 1. Ganciclovir molecular weight is 255.23 g/mol with a molecular formula of $C_9H_{13}N_5O_4$. It is a white crystalline powder and soluble in Hydrochloric acid, water, methanol, ethanol, and dimethyl sulphoxide and melts between 248-249 °C. There were a number of literature on analytical methods of ganciclovir are available. Present article describes various Visible, UV spectrophotometric, spectrofluorimetric and reverse phase high performance liquid chromatographic (RP-HPLC) methods reported since 2010 for the quantification of ganciclovir in bulk and its formulations.

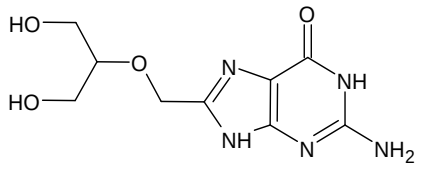

Figure 1. The chemical structure of Ganciclovir

2. Analytical Methods for ganciclovir

2.1 Visible spectroscopic methods

Naraparaju Swathi *et al.*, reported a redox-based spectrophotometric method for the quantification of Ganciclovir in pure and in its formulation [3]. The resulting complex shown absorption maxima at 510.0 nm. The method was established using 0.1 M HCl as solvent and a mixture of 0.3% w/v ferric chloride and 0.5% w/v 1,10-phenanthroline was selected as chromogenic reagent by optimization. Beer-Lambert's law obeyence was noted between 5.0-30.0 µg/mL for Ganciclovir. The method was proved to be sensitive by its low limit of detection and quantification values (0.30 and 0.90 µg/mL, respectively). The %assay value 99.2 indicated the successful implementation of the methodology in the pharmaceutical formulation.

A colorimetric method based on the diazo coupling reaction between diazotized ganciclovir and acidified *p*-dimethylaminobenzaldehyde was developed and validated [4]. The yellow-colored product generated in an alcohol medium upon coupling reaction has shown optimal wavelength at 404 nm. Linear correlation was obtained at concentrations of 10.3 - 25.7 µg/mL. The methodology was found to be accurate and precise as per validation studies. The limit of detection and quantification were noted as 0.23 and 0.70 µg/mL, respectively. No statistical difference between developed and literature methodology was observed in the assay studies.

A simple and rapid spectrophotometric method based

on the proton transfer reaction of ganciclovir with quinalizarin reagent in aqueous solution was developed for the determination of Ganciclovir [5]. The method yielded a violet product which shown maximum absorbance at 560 nm. Beer's law was obeyed in the concentration range 1-20 µg/mL. The LOD and LOQ of the method were computed as 0.21 and 0.71 µg/mL. Further, the methodology was justified with the validation variables and determination of ganciclovir in the marketed formulation.

Two colorimetric methods have been developed for the quantitative estimation of Ganciclovir [6]. One of the method is based on the reaction of amino group of Ganciclovir with *p*-dimethyl amino benzaldehyde, forming a greenish yellow colored complex, which shown absorption maximum at 401 nm. The linearity was found to be over the concentration range 80–200 µg/mL. The second method is based on the reaction with 1,2-naphtha quinine-4-sulphonic acid sodium salt (Folin's Reagent), which exhibited absorption maximum at 544 nm. Linearity in this method was noted between concentration range 4–14 µg/mL. both the methods are validated as per ICH guidelines and statistically proved significant.

A simple and sensitive spectrophotometric method based on reduction of potassium permanganate by ganciclovir in alkaline medium was developed for the determination of ganciclovir in bulk and in formulation [7]. A green colour product with absorption maximum 610 nm was formed during the analysis Beer's law was obeyed in the concentration range 2-100 µg/mL. The LOD and LOQ of the methodology was observed as 0.21 and 0.72 µg/mL, respectively. Compatable and significant results were obtained, when the methodlogy was adopted in the determination of the drug in marketed formulations.

A colorimetric method has been developed and validated based on reaction with Folin-Ciocalteu reagent in presence of alkali to form intense blue color chromogen exhibiting absorption maximum at 764.7 nm [8]. The method obeyed Beer's law in the concentration range of 50-250 ng/mL. The outcomes

of the validation studies were found to be satisfactory. The proposed methods are simple, rapid and suitable for the routine quality control application.

2.2 UV-spectrophotometric methods

A UV absorption-based method is developed and validated by dissolving the analyte in 0.1 M hydrochloric acid [9]. The linearity was obtained between the concentration range of 2-16 µg/mL with correlation coefficient of 0.999 when measured at 255 nm. The percentage recovery of Ganciclovir ranged from 100.11 to 100.48 %. The developed method is validated as per ICH guidelines and % RSD values were proved to be statistically significant.

A simple spectrophotometric method was developed and validated by dissolving the analyte in chloroform [10]. The methodology has shown linearity in the range of 1-40 µg/mL, when measurement was done at 240 nm. The outcomes of the validation studies was in line with the specifications of ICH.

In the same paper [8], two economical spectrophotometric methods have been developed and reported. First method is based on the first order derivative spectroscopy, in which derivative amplitude was measured at 238 nm (n=1). The second method is based on calculation of area under curve for analysis of ganciclovir in wavelength range of 245-255 nm. The drug follows Beer's law in the concentration range of 5-25 ng/mL in both methods.both the methods were validated and the results were in accordance with the ICH specifications.

2.3 Spectrofluorimetric method

An affordable spectrofluorimetric method was developed and validated for the estimation of ganciclovir in bulk and marketed formulation [11].The method established based on measuring the native fluorescence of ganciclovir in 0.2 M hydrochloric acid buffer of pH 1.2 at 374 nm after excitation at 257 nm. Rectilinear nature of calibration graph was noticed in the concentration range of 0.25–2.00 μg/mL. The limit of quantification and limit of detection were found to be 0.029 and 0.010 μg/mL, respectively. The methodology was validated as per ICH guidelines and the procedure was demonstrated to be accurate, precise, and reproducible based on the outcomes.

2.4 High performance liquid chromatographic methods

A isocratic RP-HPLC assay technique has been developed for for Ganciclovir in its drug substance [12]. The separation was completed using Hypersil BDS C18, column and a mixture of phosphate buffer (0.01 M, pH: 5.3) and acetonitrile 70:30 (v/v) as mobile phasewith a flow rate of 1.0 mL/min. The detection was achieved at 245 nm. The analyte was subjected for various stability studies. a linear detector result was observed between 20 - 30 µg/mL with a correlation coefficient coefficient of 0.9999. The validation of the methodology was performed and the outcomes were found to be in accordance with ICH specifications.

A simple and gradient RP-HPLC method has been developed for the determination ofganciclovir in pharmaceuticals [13]. Chromatographic separation was achieved by using inertsil ODS C18 column (4.6 mm × 250 mm, 5.0 µm) and ammonium acetate buffer, sodium salt of hexane sulfonic acid as ion-pairing reagent in 1000mL water, and acetonitrile (90:10) (v/v) as mobile phase at a flow rate of 1.0mL/min. The analyte peaks were obtained upon UV detection at 245 nm at column temperature (30 ◦C). The method was found to be linear over the range of 0.02–75 µg/mL. The LOD and LOQ were computed as 4.1 and 20 ng/mL, respectively. The method was successfully extended to study its stability. The accuracy and the precision of the method were found to be significant as per ICH guidelines.

A reversed phase high-performance liquid chromatographic (RP-HPLC) method involving a simple protein precipitation procedure with no solid-phase or liquid–liquid extraction was reported for ganciclovir plasma concentrations in cytomegalovirus infectious infants with hearing loss [14]. The chromatographic separation was achievd by using a Cadenza CD-C18 column with phosphate buffer (pH 2.5, 25 mM) containing 1% methanol–acetonitrile mixture (4:3, v/v) as a mobile phase at a 0.7 mL/min flow rate. The analyte was detected using a fluorescence detection at emission 380 nm after excitation at 265 nm. The LOD and was obtained as 0.025 µg/mL for 100 µL of plasma sample. The validation studied was found to be satisfactory.

A cost effective HPLC method was achieved by using a pre-packed Phenomenex C-18 (250 × 4.6 mm, 5 µm) column with acetonitrile and 10 mM potassium dihydrogen orthophosphate buffer (pH 5.0 ± 0.05; 5: 95, v/v) as mobile phase [15]. The detection was carried out at 252 nm by maintain the flow rate of mobile phase at 1 mL/min. The method

is linear with correlation of coefficient greater than 0.998. Percentage RSD in all the validation parameters was found to be within ICH specifications.

A RP-HPLC method developed using Oyster column and combination of trifluoro acetic acid buffer and methanol at pH 2.5 (80:20) at f flow rate of 1 mL/min. When the detection was done at 254 nm, the retention time of ganciclovir was observed as 5.823 min in comparison with the internal standard (acyclovir: 7.107 min). The linear response was noticed at 12-72 µg/mL range, when column temperature is maintained at 30 ℃. As per the results of validation and assay, the method was found to be simple, precise and rapid [16].

3 CONCLUSIONS:

A number of analytical methods for the quantification of Ganciclovir were consulted and details were provided in this article. Visible spectroscopic methods developed based on reaction of ganciclovir with various chromogenic reagents affords colored products, which showed absorption maximum at a particular wavelength. Spectrofluorimetric methods offer greater sensitivity over UV methods, as measurement at two wavelengths is possible by using them. The HPLC methods, in addition to their high accuracy and precision, they offer greater flexibility in the selection of stationary and mobile phases. By implementation of various extraction procedures, this feature may be useful in the quantification of ganciclovir in biological fluids.

4 REFERENCES:

1. Goodrich JM, Mori M, Gleaves CA, Du Mond C, Cays M, Ebeling DF, Buhles WC, DeArmond B, Meyers JD. Early treatment with Ganciclovir to prevent cytomegalovirus disease after allogeneic bone marrow transplantation. The New England Journal of Medicine. 1991; 325(23): 1601-1607.
2. Ganciclovir IUPAC name (accessed on December 2023), Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Ganciclovir#section=Names-and-Identifiers.
3. **Swathi N**, Asra Jabeen, Barla Karuna Devi and Anumolu Durga Pani Kumar. Redox-based Spectrophotometric Method for the Determination of Ganciclovir in Bulk and Pharmaceutical Dosage Form. International Research Journal of Pure and Applied Chemistry. 2023; 24(2):9-18. Doi: https://doi.org/10.9734/irjpac/2023/v24i2804
4. Thomas OE, Adegoke OA. Development of a visible spectrophotometric method for the analysis of Ganciclovir in bulk sample and dosage form. Tropical Journal of Pharmaceutical Research. 2015; 14(6): 1095-1101.
5. Usra I. S.AI-Neaimy and Amal M. S.AI-Delmyi. Visible spectrophotometric determination of Ganciclovir in its pharmaceutical formulation using quinalizarin reagent. Jordan Journal of chemistry. 2013;8(2):103-112.
6. Anil Kumar T, Grupadayya BM, Rahul Reddy MB. Selective and validated spectrophotometric methods for determination of Ganciclovir with PDAB and Folin's reagents. Indian Journal of Chemical Technology. 2012; 19: 56-62.
7. AL-Neaimy UI, Hamdon EA. The use of oxidation reaction for the spectrophotometric determination of Ganciclovir in pharmaceutical formulations. Raf Journal of Sciences. 2012; 23(4): 93-104.
8. Sarsambi PS, Sonawane A, Malipatil SM, Basavraj H, Faheem A. Spectrophotometric estimation of Ganciclovir in bulk drug and its formulation. International Journal of PharmTech Research. 2010; 2(2): 1264-1268.
9. Madhusudhana RG, Jose Gnana Babu C, Tamizh Mani T. Validated spectrophotometric estimation of Ganciclovir in pure and capsule dosage form. Imperial Journal of Interdisciplinary Research. 2017; 3(1): 368-370.
10. Bhaskar Reddy CM, Subba Reddy GV. Determination of Ganciclovir in bulk and pharmaceutical dosage forms by UV spectrophotometric method. International Research Journal of Pharmacy. 2012; 3(8): 286-288.
11. Garima B, Emil J, Satish Reddi, Vibhu N, Ranendra NS. Rapid, simple and sensitive spectrofluorimetric method for the estimation of Ganciclovir in bulk and pharmaceutical formulations. Journal of Spectroscopy. 2013; 2013: Article ID 972806.
12. Madhusudan P, Venkateshwar Reddy K, Surinderpal Singh. Determination of assay and validation of stability indicating RP-HPLC method for Ganciclovir in nciclovir drug substance. International Journal of Scientific & Technology Research. 2020; 9(2): 4191-4195.
13. Ramesh PJ, Basavaiah K, Vinay KB, Xavier CM. Development and validation of RP-HPLC method for the determination of Ganciclovir in bulk drug and in formulations. International Scholarly Research Network. 2012; Article ID 894965.
14. Yoshida T, Takahashi R, Imai K, Ichida H, Arai Y, Oh-ishi T. A simple, sensitive determination of Ganciclovir in infant plasma by High-Performance liquid chromatography with

fluorescence detection. Journal of Chromatographic Science. 2010; 48: 208-211.
15. Ashok Kumar P, Chandrakant B, Ashok P, Mahesh P. Analytical method development and validation of Ganciclovir API by high performance liquid chromatography. International Journal of Chemical and Analytical Science. 2010; 1(10): 221-223.
16. Sarsambi PS, Sonawane A, Faheem A. Development and validation of RP-HPLC method for the determination of Ganciclovir in bulk drug and its formulations. International Journal of Pharma and Bio Sciences. 2010; 1(2).