https://doi.org/10.51483/AFJPS.1.1.2021.40-46 ISSN: 2789-5092

SvedbergOpen
DISSEMINATION OF KNOWLEDGE

African Journal of Pharmaceutical Sciences

Publisher's Home Page: https://www.svedbergopen.com/

Research Paper Open Access

Design and Validation of UV Spectrophotometric Method for Estimation and the Routine Quality Control Analysis of Sildenafil Citrate in Bulk and in Tablet Formulations

Mahmoud A. Ibrahim[1], Fatehalrahman F. Magbool[2*], Abdrhman Mahmoud Gamil[3] and Mohamd E. Adam[4]

[1]College of Pharmacy, Department of Pharmaceutical Analysis, Ribat National University, Sudan. E-mail: mahmoudbutre@gmail.com
[2]Department of Pharmaceutics, Faculty of Pharmacy, Al-Neelain University, Sudan. E-mail: fmagbool@yahoo.com
[3]Department of Pharmaceutics, Faculty of Pharmacy, Al-Neelain University, Sudan. E-mail: Abdrahmangamil@gmail.com
[4]Department of Chemistry, Faculty of Pharmacy, University of Khartoum, P.O. Box 1998, Khartoum, Sudan. E-mail: dackouk2015@gmail.com

Article Info

Volume 1, Issue 1, September 2021
Received : 10 February 2021
Accepted : 16 July 2021
Published : 05 September 2021
doi: 10.51483/AFJPS.1.1.2021.40-46

Abstract

A Simple, sensitive, specific, UV Spectrophotometric method has been designed and developed for the determination of sildenafil citrate in bulk power and in pharmaceutical dosage form as well as its application for the routine quality control analysis of Sildenafil in bulk as well as in tablet formulations. The optimum condition for the analysis of the drug was established. Sildenafil citrate exhibiting absorption at 295 nm. The proposed method exhibited good levels of detection and quantitation. The specificity of the method was determined by checking the interference of placebo with analyte. There was no interference is observed. The regression equation for the Beer-Lambert's plot of pure Sildenafil citrate was found to be; $Y = 0.190\ x$ and the correlation coefficient (R^2) of 0.9990. The Beer's plot was obeyed in concentration range between 0.001-0.005 mg/mL. There is good correlation between absorbance and concentration. Which is the basis of this method of analysis. The repeatability and intermediate precision were also assessed. The developed method was found to be precise as the % RSD values. The application of the validated method to the three brands showed that all brands had values within the range specified in the IP (90-110%). The results and the statistical parameters demonstrate that the proposed UV spectrophotometric method is simple, rapid, specific, accurate and precise. Since the method can be used for estimation and routine quality control of Sildenafil in bulk as well as in tablet formulations.

Keywords: *Sildenafil citrate; UV Spectrophotometric method, Validation, Correlation coefficient, Quality control*

1. Introduction

Sildenafil chemically named as 1-[4-ethoxy-3-(6, 7-dihydro-1-methyl-7-oxo-3- propyl-1*H*-pyrazolo [4, 3-*d*] pyrimidin-5-yl) phenylsulfonyl]-4-methylpiperazine citrate [M. wt. 666.6 g/m mole], is an anti-impotent drug and a selective inhibitor

* *Corresponding author: Fatehalrahman F. Magbool, Department of Pharmaceutics, Faculty of Pharmacy, Al-Neelain University, Sudan. E-mail: fmagbool@yahoo.com*

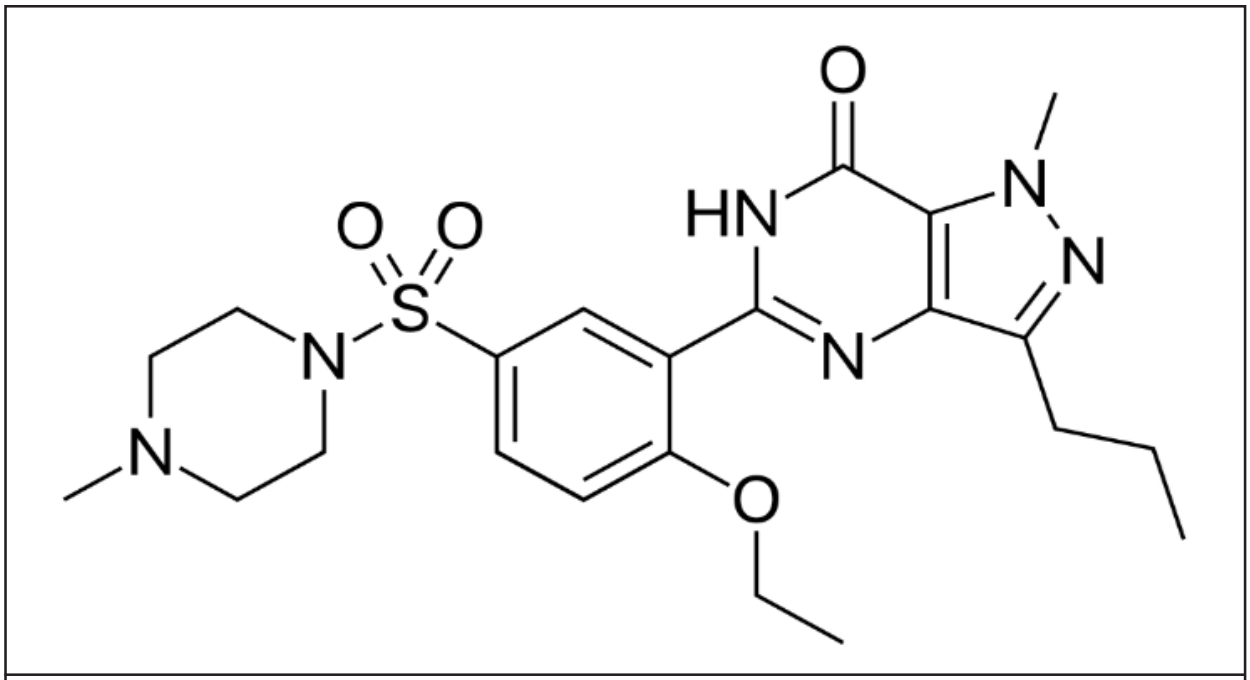

Figure 1: Sildenafil Chemical Structure

of cyclic guanosine monophosphate (cGMP) specific phosphodies-terase type 5 (PED5). The chemical structure of sildenafil (Corbin and Francis, 1999; Card *et al.*, 2004; and Al-Omari *et al.*, 2006) is shown in Figure 1.

Sildenafil, rapidly absorbed after oral administration, with absolute bioavailability of about 40% its pharmacokinetics are dose-proportional over the recommended dose range. It is eliminated predominantly by hepatic metabolism and is converted to an active metabolite with properties similar to the parent, Sildenafil (Al-Omari *et al.*, 2006).

Sildenafil, when used properly, is relatively safe. There are, however, certain side effects that could create potential hazards. For example, Sildenafil has been shown to potentiate the hypotensive effects of nitrates commonly employed in the treatment of certain heart conditions (Kloner and Jarow, 1999). Moreover, while sildenafil inhibits PDE5, it also has a high affinity for phosphodiesterase type 6 (PDE6), which is a retinal enzyme involved in photo-transduction (Pfizer Inc., 1998). The inhibition of PDE6 can result in the inability to discriminate between blue and green colors, resulting in a condition known as “blue tinge” (Toxi-News, 1999). Although only about 3% of patients report visual disturbances, this blue-green impairment could cause problems in the execution of certain tasks. Because of its increasing popularity and potential side-effects, the need for a procedure to detect sildenafil content uniformity in pharmaceutical dosage forms are becoming increasingly important.

USP describes HPLC method for the examine sildenafil citrate (The United States Pharmacopeia (USP 35), 2012). Sildenafil citrate was determined by different methods including HPLC in pharmaceutical products (Abd-ELbary *et al.*, 2004; and Molleti *et al.*, 2013). HPLC in Pharmaceutical products with other drugs (Kalyani *et al.*, 2014; and Fidan *et al.*, 2016), HPLC in dietary supplements (Li *et al.*, 2017), CGC in pharmaceutical formulations and dietary supplements (Berzas *et al.*, 2002; and Mokhtar *et al.*, 2016), HPTLC in commercial lifestyle products (Do *et al.*, 2015), electroanalytical methods in pharmaceutical preparations (Batista *et al.*, 2010; Güzel *et al.*,2014; and Farghali *et al.*, 2015) and flow injection analysis in tablets using UV-detection (Altiokka *et al.*, 2001) and amperometric detection (Lopes *et al.*, 2012).

Until today, no official UV-V is spectroscopic method of analysis for the estimation of Sildenafil was present in any of the pharmacopeias, it was necessary to try to develop a method that is suitable for the identification and quantification of such a drug. Availability of UV-V is spectrophotometer in many laboratories and the simplicity of analytical procedures make the technique very attractive tool for wide range of applications, including detection of metals and analyses of organic compound such drugs and medicaments. Therefore, the present work aims at developing a simple and rapid spectrophotometric method for the determination of sildenafil citrate in bulk power and in pharmaceutical dosage form as well as its application for the routine quality control analysis of Sildenafil in bulk as well as in tablet formulations.

2. Materials and Methods

2.1. Apparatus and Instrumentation

Glassware (Iso Lab) Germany, Double Beam UV Spectrophotometer, (T80) PGT80, England, Sensitive Balance (Kern) Germany, Ultra Sonicator (China), Centrifuge (Braun) UK.

2.2. Chemicals

Reference Sildenafil was a kind gift sample from Tabuk pharmaceuticals-Sudan. Three different marketed brands/ samples of Sildenafil citrate tablets (50 mg) were purchased from community pharmacies (drug store) in Khartoum city, Sudan. The samples were properly checked for their drug dose, manufacturing license number, batch numbers, manufacturing and expiry dates. They were coded as F1, F2 and F3 (Table 1). Ethanol (Scharlau) Spain.

Pharmaceutical grade of Sildenafil was procured from Tabuk pharmaceuticals-Sudan. All the chemicals were of analytical reagent grade of Merck (Germany) unless otherwise specified. Ethanol was used to prepare all solutions. Freshly prepared solutions were always employed. Different brands of tablets of Sildenafil Citrate were supplied from local pharmacy.

2.3. Method

2.3.1. Preparation of Standard Solution

Standard stock solution was prepared by dissolving 50 mg of Sildenafil in 50 mL of ethanol to get concentration of 1000 µg/mL solution. It was further diluted to get working standard solution of 100 µg/mL.

2.4. Method Development

2.4.1 Development and Optimization of the Spectrophotometric Method

Proper wave length selection of the methods depends upon the nature of the sample and its solubility. To develop a rugged and suitable spectrophotometric method for the quantitative determination of Sildenafil, the analytical conditions were selected after testing the different parameters such as solvents, wavelength, and other spectroscopic conditions. Our preliminary trials using different solvents. By using ethanol as solvent 99.5% v/v best result was obtained.

2.5. Selection of Wavelength

Scan standard solution in UV spectrophotometer between 200 nm to 400 nm on spectrum mode, against ethanol as blank after baseline correction. Which shows the maximum absorbance at 295 nm. The same λ_{max} was used for the further measurement of the drug.

2.6. Preparation of Calibration Curve

Working solutions were prepared from standard stock solution by further dilution with ethanol to get concentration of 1, 2, 3, 4 and 5 µg /mL. Finally, the prepared standards were measured after standing for 5.0 min at λ_{max} as recorded in Table 1, in each case against a solvent ethanol as blank. A calibration graph of the absorbance *versus* the concentration of the drug was plotted (Table 2 and Figure 2).

2.7. Method Validation

Validation of the analytical method for the determination of Sildenafil citrate in pure form and in pharmaceutical formulation was carried out as per ICH guidelines with regard to system suitability, linearity, accuracy, precision, LOD, LOQ, and sensitivity as follows.

Table 1: The Selected Brands of Sildenafil in Sudan Drug Market

Brand Code-Strength	Country of Origin
F1-50 mg	Sudan
F2-50 mg	Jordan
F3-50 mg	Egypt

Table 2: Absorbance Data of Standard Sildenafil

STD Sildenafil Concentration µg/ml	Absorbance at 295 nm
1	0.175
2	0.363
3	0.566
4	0.778
5	0.958

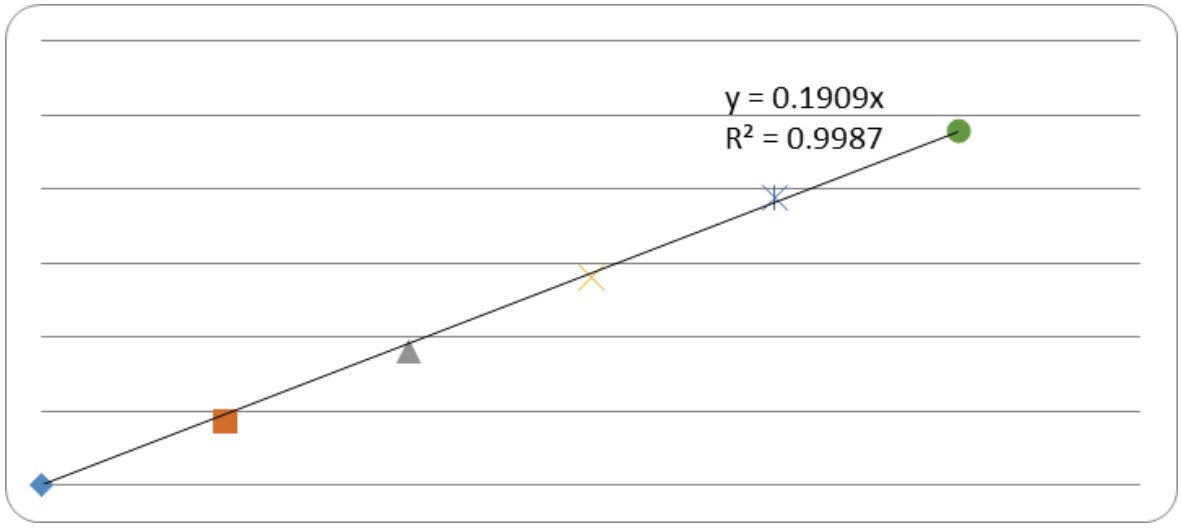

Figure 2: STD Calibration Curve Sildenafil in Ethanol

2.8. Specificity

Specificity of an analytical method is its ability to measure the analyte accurately and specifically in the presence of component that may be expected to be present in the sample matrix. The specificity of the method was determined by checking the interference of placebo with analyte.

2.9. Linearity

The method was validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision and of the analyte (Vessman, 1996). For Sildenafil citrate, five-point calibration curves were generated with the appropriate volumes of the working standard solutions for UV method.

2.10. Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions (Baokar *et al.*, 2011).

2.11. Accuracy

The accuracy of an analytical method is the closeness of the test results obtained by that method to the true value (Shrikrishna *et al.*, 2011). The accuracy of an analytical method is defined as the degree to which the determined value of analyte in a sample corresponds to the true value.

2.11.1. Application of Validated UV Spectrophotometric Method for Assay of Sildenafil Citrate Tablet Formulations

For analysis of commercial formulations, twenty tablets containing Sildenafil citrate were taken and powdered. Tablet powder equivalent to 50 mg of Sildenafil citrate was transferred to 50 mL volumetric flask and dissolved in ethanol. Then

the solution was sonicated for 15 min and filtered through Whatman filter paper No. 41 and it was further diluted to get the required concentration. The absorbance of the prepared sample solution was measure against methanol as a blank at 295 nm. A standard additions technique was also used to confirm the accuracy and precisions.

3. Results and Discussion

Since analysis is an important development and quality control of any dosage form, it necessary to have a simple, precise, accurate and sensitive method for assay of any drug product both as a bulk and in its formulation (Rao *et al.*, 2010). Simple UV method has become necessary for the assay of this drug because, UV unlike HPLC is simple, rapid and readily available in many poor countries of the world. This will also help to checkmate influx of fake and adulterated products into the drug market. As an alternative to existing standard methods, we propose a procedure to determine Sildenafil drug substance based on UV spectrophotometry.

The proposed method exhibited good levels of detection and quantitation. The specificity of the method was determined by checking the interference of placebo with analyte. There was no interference is observed. The linearity of the drug was found to be between 1-5 µg/mL concentrations. The regression equation for the Beer-Lambert's plot of pure Sildenafil citrate was found to be; $Y = 0.190\,x$ and the correlation coefficient (R^2) *of 0.9990* (Figure 2 and Table 3). The Beer's plot was obeyed in concentration range between 1-5 µg/mL. There is good correlation between absorbance and concentration, which is the basis of this method of analysis.

The result of precision study are shown in Table 3. The developed method was found to be precise as the % RSD values. The results also indicated that tablet excipients usually present during compounding are not likely to interfere with the absorption spectrum of Sildenafil citrate.

The application of the validated method to the three brands showed that all brands had values within the range specified in the IP (90-110%) (British Pharmacopoeia, 2015), (Table 4), the results and the statistical parameters demonstrate that the proposed UV spectrophotometric method is simple, rapid, specific, accurate and precise.

Table 3: Regressions Data of Sildenafil Citrate

Parameter	F1	F2	F3
Wave length	295	295	295
LOD	0.1 µg/ ml		
LOQ	0.3 µg/ ml		
Regression Equation	Y = 0.190 x		
Correlation Coefficient	0.9990		
Inter day precisions RSD%	0.663327	0.375995	0.237818
Intraday precisions RSD%	0.99156	0.99173	0.99895

Table 4: Determination and Assay of Sildenafil Citrate Studied Brands Content % by Proposed Method

Sample Conc. µg/ ml	Amount Found	Recovery %	RSD %
F1	0.365	96 %	0.99156
F2	0.384	101 %	0.99173
F3	0.345	92,10 %	0.99895

4. Conclusion

In this study a simple, rapid, sensitive, accurate and precise UV spectrophotometric method for the determination of Sildenafil in bulk and pharmaceutical formulation has been developed and validated. It was found that the common excipients present in the formulation did not interfere with the proposed method and can be used for the routine quality control analysis of Sildenafil in bulk as well as in tablet formulations.

Acknowledgment

The authors are thankful to wish to Tabuk Pharmaceuticals, Khartoum, Sudan, for providing the gift sample of Sildenafil (standard).

References

Abd-ELbary, A., *et al.* (2004), Stability Indicating High Performance Liquid Chromatographic Assay for the Determination of Sildenafil Citrate in Bulk and in Formulations. *Chromatographia* 59(9-10), 561-566.

Al-Omari, M.M., Zughul, M.B., Davies, J.E.D., and Badwan, A.A. (2006). Sildenafil/Cyclodextrin Complexation: Stability Constants, Thermodynamics, and Guest-host Interactions probed by 1H NMR and Molecular Modeling Studies. *J Pharm Biomed Anal*., ;41, 857-65.

Altiokka, G. *et al*. (2001), FIA of Sildenafil Citrate using UV-detection. *Journal of Pharmaceutical and Biomedical Analysis,* 25(2), 339-342.

Baokar, Shrikrishna., Pawar, Vinod., and Sonawane, S.H. (2011). High Performance Liquid Chromatographic Method Development and Validation of Cholesterol Inhibitor Drug.*Journal of Pharmacy Research*, 4(7), 2313-2316.

Batista, E.F. *et al*. (2010). Differential Pulse Voltammetric Determination of Sildenafil Citrate (Viagra) In Pharmaceutical Formulations Using a Boron-doped Diamond Electrode. *Analytical Letters*, 43(2010), 1046-1054.

Berzas, J.J. *et al.* (2002). Validation of a Capillary Gas Chromatographic Method for the Determination of Sildenafil Citrate in its Pharmaceutical Formulations (Viagra). Experimental Design for Evaluating the Ruggedness of the Method. *Chromatographi,a,* 55(9/10), 601-606.

British Pharmacopoeia. (2015). *British Pharmacopoeia Commission,* London. 3, 320.

Card, G.L, England, B.P., Suzuki, Y., Fong, D., Powell, B., Lee, B. *et al.* (2004). Structural Basis for the Activity of Drugs that Inhibit Phosphodiesterases. *Structure*,12, 2233-47.

Corbin, J.D., and Francis, S.H. (1999). Cyclic GMP Phosphodiesterase-5: target of Sildenafil. *J Biol Chem*., 274, 13729-32.

Do, T.T. *et al*. (2015). Simultaneous Detection of Three Phosphodiesterase Type 5 Inhibitors and Eight of Their Analogs in Lifestyle Products and Screening for Adulterants by High-performance Thin-layer Chromatography. *Journal of AOAC International,* 98(5),1226-1233.

Farghali, R.A. *et al*. (2015). Gold Nanoparticles-modified Screen-printed Carbon Electrode for Voltammetric Determination of Sildenafil Citrate (Viagra) in Pure Form, Biological and Pharmaceutical Formulations. *International Journal of Electrochemical Science,* 10(2), 1494-1505.

Fidan, A.K. *et al.* (2016). Simultaneous Determination of Sildenafil and Tadalafil in Legal Drugs, Illicit/Counterfeit Drugs, and Wastewater Samples by High-performance Liquid Chromatography. *Journal of AOAC International,* 99(4), 923-928.

Güzel, R. *et al.* (2014). New Voltammetric Approach to the Quantitative Estimation of Sildenafil Citrate in Tablets Using Disposable Pencil Graphite Electrode. *Sensor Letters,* 12(11), 1675-1681.

Kalyani, K. *et al.* (2014). A Novel Stability indicating RP-HPLC Method for the Simultaneous Estimation of Sildenfii Citrate and Dapoxetine Hydrochloride in Bulk and Pharmaceutical Formulations. *Der Pharmacia Letter,* 7(10), 98-106.

Kloner, R.A., and Jarow, J.P. (1999). Erectile Disfunction and Sildenafil Citrate and Cardiologists. *Am J Cardiol.*, 83(4), 576-82.

Li, J. *et al*. (2017). Solid-phase Extraction Assisted Dispersive Liquid Liquid Microextraction Based on Solidification of Floating Organic Droplet to Determine Sildenafil and Its Analogues in Dietary Supplements. *Journal of Separation Science*, 40(3), 3120-3129.

Lopes, Júnior, A.C.V. *et al.* (2012). Determination of Sildenafil Citrate (Viagra®) in Various Pharmaceutical Formulations by Flow Injection Analysis with Multiple Pulse Amperometric Detection. *Journal of Brazilian Chemical Society* 23(1), 1800-1806.

Mokhtar, S.U. *et al*. (2016). Rapid Determination of Sildenafil and its Analogues in Dietary Supplements Using Gas Chromatography Triple Quadrupole Mass Spectrometry. *Journal of Pharmaceutical and Biomedical Analysis,* 121(2016), 188-196.

Molleti, S. *et al*. (2013). Determination of Sildenafil Citrate and its Related Substances in the Commercial Products and Tablet Dosage Form Using RP-UPLC. *American Journal of PharmTech Research,* 3(2), 378-404.

Pfizer Inc. (1998). Viagra: compound data sheet. Pfizer Inc.

Rao, N., Bagyalakshmi, J., and Ravi, T. (2010). *Chem. Pharm. Res*., 2(2), 350-356.

Shrikrishna, B., Baokar, B., Shirke, V., and Sivanand, G.K. (2011). Pratheesh, Analytical Method Development and Validation for Esteemation of Sildenafil Citrate From Tablet Dosage Form by RP-HPLC. *Int. J. Res. Phar.Sci*. 2(2), 130-136.

The United States Pharmacopeia (USP 35). (2012). The National Formulary (NF 30), 5994.

Toxi-News. (1999). Sildenafil (ViagraÒ). TOXI-LAB, Irvine, CA, 18(1), 1.

Vessman, J. (1996). Selectivity or Specificity? Validation of Analytical Methods from the Perspective of an Analytical Chemist in the Pharmaceutical Industry. *J. Pharm and Biomed. Anal*., 14, 867-869.

Cite this article as: Mahmoud A. Ibrahim, Fatehalrahman F. Magbool, Abdrhman Mahmoud Gamil and Mohamd E. Adam (2021). Design and Validation of UV Spectrophotometric Method for Estimation and the Routine Quality Control Analysis of Sildenafil Citrate in Bulk and in Tablet Formulations. *African Journal of Pharmaceutical Sciences*, 1(1), 40-46. doi: 10.51483/AFJPS.1.1.2021.40-46.