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: \( Y = 0.190 \times \) 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

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1. Introduction

Sildenafil chemically named as 1-(4-ethoxy-3-(6, 7-dihydro-1-methyl-7-oxo-3- propyl-1H-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.
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 phototransduction (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 $\lambda_{max}$ 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 $\lambda_{max}$ 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 |
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 measured 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 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: \( Y = 0.190 \times \) and the correlation coefficient \( (R^2) = 0.9990 \) (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.

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<th>Table 3: Regressions Data of Sildenafil Citrate</th>
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<td>Parameter</td>
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<td>Intraday precisions RSD%</td>
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<th>Table 4: Determination and Assay of Sildenafil Citrate Studied Brands Content % by Proposed Method</th>
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<td>Sample Conc. μg/mL</td>
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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.

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References


