



DEVELOPMENT OF ACID–BASE TITRIMETRIC METHOD FOR DETERMINATION OF SILDENAFIL CITRATE IN BULK AND TABLETS FORMS

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ABSTRACT

A simple acid –base titrimetric method was developed for the determination of Sildenafil citrate (SC) in bulk and tablet dosage forms. The method was based on titration of SC against 0.01MNaOH using phenolphthalein as indicator. The method was validated with respect to the linearity, precision and accuracy. Calibration curve was found to be linear ($r= 0.999$) in a range of 5-25mg. The repeatability and inter-day precision were of RSD% values 1.01 and 0.47, respectively. The accuracy of the method was confirmed by the obtained recovery % values (99.7, 99.9 and 100.3 for levels of 50%, 100% and 150%, $n=3$).

KEYWORDS: Sildenafil Citrate; Titrimetric Method; Recovery.

INTRODUCTION

Sildenafil Citrate (figure 1) is a pyrazolo-pyrimidinyl-methylpiperazine derivative. It is frequently prescribed medication used in the treatment of erectly dysfunction.^[1] It is a potent and competitive inhibitor of the type-V cyclic guanosine monophosphate (cGMP) specific phosphodiesterase enzyme, the predominant isoenzyme in the human corpus cavernosum.^[2,3]

Several analytical methods have been reported for determination of Sildenafil Citrate, which include chromatographic and spectrophotometric methods.^[4-13]

To best of our knowledge, there is no pharmacopoeial method for the assay of Sildenafil Citrate.

Therefore, it is deemed useful to develop a simple volumetric method for its assay in pharmaceutical dosage forms.

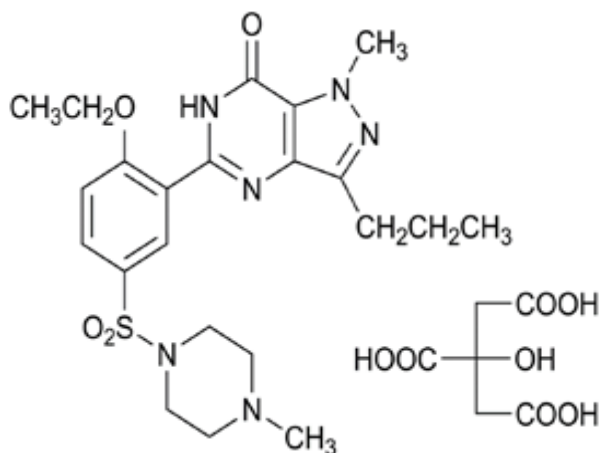


Fig. 1: Chemical structure of Sildenafil Citrate.

MATERIALS AND METHODS

Materials

SC working standard was kindly provided by Azal-Sudan laboratories, Sodium Hydroxide (LOBA Chmei), Absolute Ethanol (PROLABO), Potassium Hydrogen Phthalate (MERCK), Phenolphthalein (MERCK).

Preparation of working solutions

Preparation of 0.01 M sodium hydroxide

Sodium hydroxide solution (0.01 M) was prepared by transferring 200mg of NaOH into 500 ml volumetric flask and then the volume was completed to 500 ml with distilled water.

Preparation of Potassium hydrogen phthalate (KHP) solution

Potassium hydrogen phthalate solution was prepared by transferring accurately weighed 204 mg of potassium hydrogen phthalate into 100 volumetric flask then dissolved in distilled water and the volume was completed to the mark with the same solvent.

Preparation of phenolphthalein (Ph-Ph) indicator

Accurately weighed Ph-Ph powder (50mg) was dissolved in 50ml absolute ethanol and the volume was then completed to 100 ml with distilled water.

Procedure

Standardization of 0.01M Sodium hydroxide

The primary standard potassium hydrogen phthalate solution was titrated against the prepared solution of sodium hydroxide using Ph-Ph as indicator then the actual concentration of 0.01M NaOH was calculated.

Volumetric analysis

An accurately weighed amount of SC standard (10mg) was dissolved in 10ml of previously neutralized ethanol, and sonicated for 15 min to enhance the solubility. Three drops of ph-ph indicator were added and titration was carried out against 0.01M NaOH to the pink color end point.

Tablet assay by the proposed method

Twenty tablets of Brand1 (100 mg SC), Brand2 (50mg SC), and Brand3 (50mg SC) were weighed accurately and ground into a fine powder. An amount equivalent to 10 mg of sildenafil citrate was weighed and transferred into a 50ml Erlenmeyer flask and dissolved in 30ml of previously neutralized ethanol, sonicated for 15 minutes to enhance the solubility. The solution was filtered using filterator pump, ph-ph indicator was added to the resultant filtrate and titration was conducted against 0.01M NaOH until the color change from colorless to pink color.

Method validation

The method was validated according to ICH guidelines in terms of linearity, accuracy, precision.

RESULTS AND DISCUSSION

Sildenafil citrate is an invaluable medication used to treat erectile dysfunction. Many methods were reported for the determination of SC in bulk and dosage forms. These methods are expensive, time consuming and required highly skilled personnel and using toxic organic solvent. Thus, development of a simple titrimetric method which utilizes less toxic and cheap solvents is preferred. The developed method was based on the acid-base reaction between the protonated amines in Sildenafil Citrate and the standard NaOH in 4:1 ratio (drug : titrant) and all calculations were based on a simple titre value formula: 1 ml of 0.01 M of NaOH will react with 1.6668 mg of the drug. Phenolphthalein was a good option as an indicator because it is sensitive, economic and gives different colors at the end point pH.

The developed method was validated according to ICH guidelines. The linearity of the method was tested over the amounts range 5-25 mg by titrating against 0.01M NaOH. Constructed calibration curve showed good correlation coefficient ($r = 0.999$) Figure 2, and the regression analysis equation was calculated.

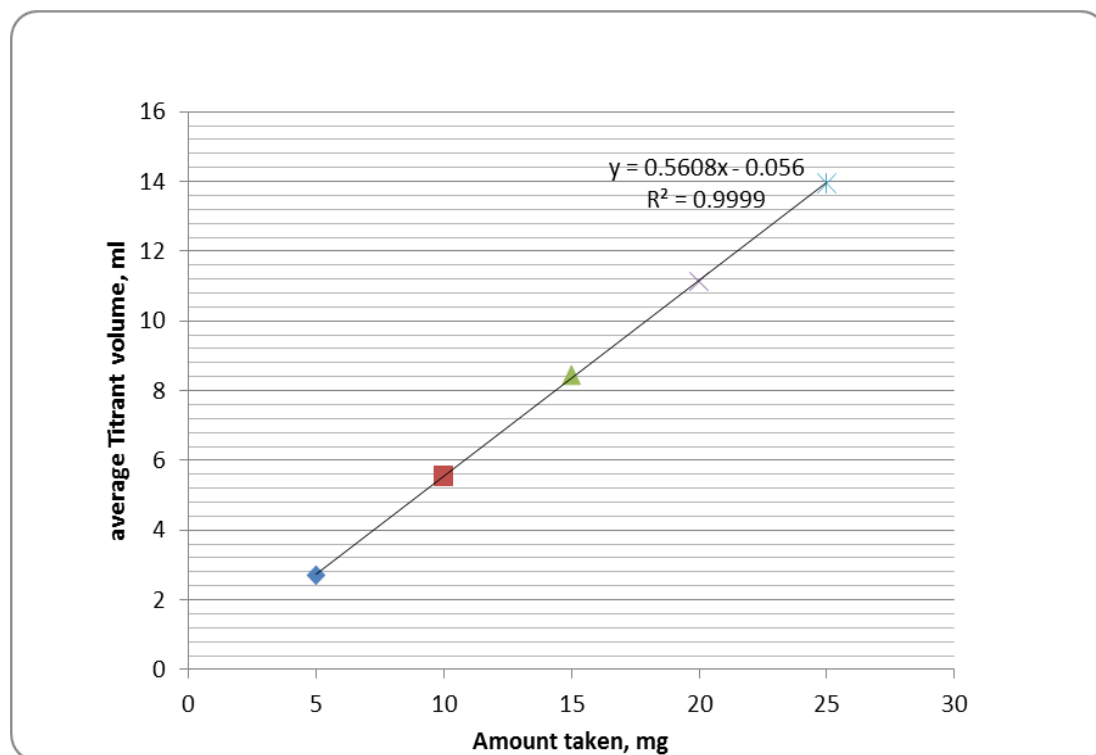


Figure 2: Linearity curve of SC working standard.

The precision of the developed method was assessed in terms of repeatability and intermediate precision by titrating replicate standard sample of 15mg of SC with 0.01M NaOH. The experiment was repeated six times in a day for repeatability and in three days for intermediate precision. The repeatability and inter-day precision were calculated and results were presented in tables 1&2. Precision of the analytical method was found to be reliable based on %RSD.

Table 1: Repeatability of the method.

Replicate No.	Corrected volume of the titrant	Mean	SD	RSD%
1	8.00	8.06	0.082	1.01
2	8.10			
3	8.10			
4	8.20			
5	8.00			
6	8.00			

Table 2: Inter-day precision.

	Mean of the corrected volume of the titrant, ml	SD	RSD%
Day 1	8.05		
Day 2	7.99	0.037	0.47
Day 3	7.98		

The accuracy of the method was confirmed by determination of the recovery using standard addition method. The drug samples were spiked at levels of 50%, 100% and 150% of test concentration. The added recovery% was calculated for each level using the following equation:

$$\text{Percent Recovery} = [(C_{\text{obs}} - \hat{C}_{\text{native}}) / C_{\text{spike}}] \times 100$$

The recovery % were 99.7, 99.9 and 100.3, n=3 at level 50%, 100% and 150% of test concentration, respectively. These results indicate the accuracy of the method and its freedom of interference of exceptions.

The titre value method was used for determination (assay) of SC in tablet dosage form. Results obtained are summarized in Table 3.

Table 3: Content percent of SC in the different brands using the proposed method.

No. of mg of SC equivalent to weight taken of dosage form	Corrected volume of titrant, ml	Percent content %
Brand 1 10	6.34	105.55
Brand 2 5	3.13	104.21
Brand 3 10	6.01	100.17

CONCLUSION

An accurate, precise and acid base titration method has been developed and validated for the analysis of Sildenafil Citrate in tablet dosage form. The percentage recovery and found concentration of active ingredient in pharmaceutical formulations showed that the amount of drug present is consistent with the labelled claim. Hence, this method is very useful simple and accurate for estimation of Sildenafil Citrate in tablet dosage forms. Furthermore, it can be utilized for determination of drugs available as citrate salts.

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REFERENCES

1. Boolell M, Gepi-Attee S, Gingell JC, and Allen MJ. Sildenafil, a novel effective oral therapy for male erectile dysfunction. *British J Urol*, 1996; 78(2): 257-261.
2. Saenz de Tejada I, Goldstein J, Blanco R, Cohen RA, Krane RJ. Smooth muscle of the corpora cavernosae: role in penile erection. *Surgery Forum*, 1985; 36(1): 623-624.
3. Aboseif SR, Lue TF. Haemodynamics of penile erection. *UrolClin North Am*, 1988; 15(1): 1-7.
4. Liu YM, Yang HC, Miao J.R. Reversed-phase HPLC determination of Sildenafil citrate tablets". *Yaowu. Fenxi. Zazhi*, 2000; 20: 61-62.
5. Lee M, Min D. Determination of Sildenafil citrate in plasma by high-performance liquid chromatography and a case for the potential interaction of grape fruit juice with Sildenafil citrate. *Ther. Drug Monit*, 2001; 23(1): 21-26.
6. Kuchekar BS, Thakkar SV, Chothe PP, Hiremath MR, Shinde DB. Spectrophotometric estimation of Sildenafil citrate in tablets. *Ind J PharmaSc*, 2005; 1: 749-751.
7. Thangabalan B, Vadivel K, Sowjanya K, Tejaswi G. Quantitative spectrophotometric determination of Sildenafil citrate in tablet formulation using urea as hydrotropic solubilizing agent. *Res J Pharm Tech*, 2011; 2(2): 235-239.
8. Reddy BPK, Reddy YR. Validation and stability indicating RP-HPLC method for the determination of Sildenafil citrate in pharmaceutical formulation and human plasma. *E-J Chem.*, 2005; 5: 1117-1122.
9. Draghmen N, Al-omari M, Badwan AA, Jaber AM. Determination of Sildenafil citrate and related substances in the commercial products and tablet dosage form using HPLC. *J Pharm Biomed Ana.*, 2001; 25: 483-492.
10. Muhamad Y H. A Simple Spectrophotometric Assay of Sildenafil In Pure and Pharmaceutical Preparations. *J Al-Nahrain University*, 2012; 15(1): 18-24.
11. Frag EYZ, Mohamed GG, Alelaiwi HMS. Utility of Ion-associate Formation Reactions for the Spectrophotometric Determination of Sildenafil Citrate in Pure form and in Virecta Tablets. *J Pharm Anal Acta*, 2011; 2(6): 131-132.
12. Sparsha. N, Ravindra Reddy. K, Venkatesh. P, Hepcykala Rani. D, Sirisha. G, Sahithireddy. P. Development of new and rapid method for UV spectrophotometric

determination of sildenafil in marketed formulations. *J Der Pharmacia Lettre*, 2012; 4(6): 1756-1759.

13. R. Kalaichelvi, G. Anusha, K. Radha, G.T. Bindhu, T. Brahmanaidu, A. Sriram Murth, G. Samuel, D. Srinivasa Rao, E. Jayachandran. Quantitative UV spectrophotometric estimation of sildenafil citrate by hydrotropic technique. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2012; 4(4): 171-172.