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ULTRA-SENSITIVE ESTIMATION OF VARDENAFIL. HCL IN PHARMACEUTICAL PREPARATIONS AND ENVIRONMENTAL WASTE WATER SAMPLES

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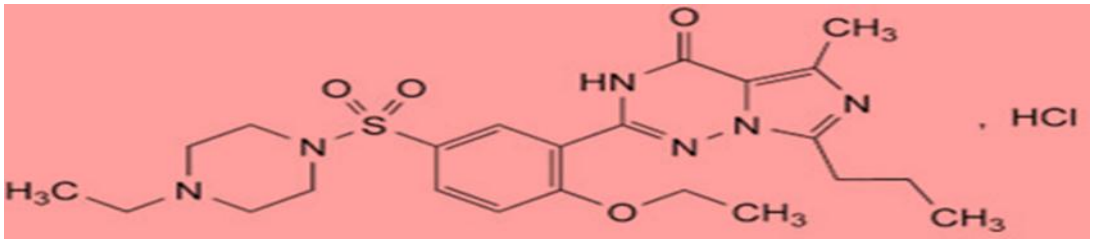
ABSTRACT
A simple, accurate, precise, rapid, economical and high sensitive UV spectrophotometric method has been developed for the estimation of vardenafil hydrochloride in pharmaceutical preparations and environmental wastewater samples, which shows maximum absorbance at 214 nm in distilled water. Beer's law was obeyed in the range of 0.1-2µg/ ml, with molar absorptivity of 4.745×10^5 $L.mol^{-1}.cm^{-1}$, relative standard deviation of the method was less than 1.9%, and accuracy (average recovery %) was 100 ± 1.03. No interference was observed from common excipients and additives often accompany with vardenafil hydrochloride in pharmaceutical preparations. The method was successfully applied to the estimation of vardenafil hydrochloride in some pharmaceutical formulations (tablets) and industrial wastewater samples. The proposed method was validated by sensitivity and precision which proves suitability for the routine analysis of vardenafil hydrochloride in true samples.

KEYWORDS: Vardenafil. HCL, Pharmaceutical Preparations, Environmental Samples, Ultraviolet.

INTRODUCTION
Vardenafil hydrochloride (VAR) chemically is **(1**-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propyli-midazo [5,1-f] [1,2,4] triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-ethylpipera-zine (Figure.1). Vardenafil is given orally as the hydrochloride trihydrate. Vardenafil hydrochloride is not official in any Pharmacopoeia, used to treat erectile dysfunction. Vardenafil inhibit phosphodiesterase type 5 (PDE-5) enzyme, which in turn maintains higher levels of cyclic guanosine monophosphate. Which relaxes smooth muscles, promotes penile blood flow and enhances erectile function.[1-3]



$C_{23}H_{32}N_6O_4S$, HCl= 525.1 g/mol
Figure 1: Chemical Structure of Vardenafil hydrochloride.

Several methods for the determination of Vardenafil hydrochloride have been described in the literature, including spectrophotometric methods[4-8], capillary electrophoretic methods[9], stability indicating LC method[10], High performance liquid chromatographic methods[11-15], and atomic emission and atomic absorption spectrometry method.[16] The present work describes a new, simple spectrophotometric method for the determination of Vardenafil hydrochloride in pure form, pharmaceutical formulations and in industrial wastewater samples. The present work describes a new, simple UV-spectrophotometric method for the determination of Vardenafil hydrochloride in pure form, pharmaceutical formulations and in industrial wastewater samples.

EXPERIMENTAL
Apparatus
Shimadzu UV- 1700 pharm aspect (double beam) spectrophotometer [Japan] with 1.0 cm quartz cells was used for absorption measurements.

Reagents
All chemical used were of analytical or pharmaceutical grade and Vardenafil hydrochloride standard material was provided from (PIONER), company for pharmaceutical industries -Iraq.

Vardenafil hydrochloride standard solution
This solution was prepared by dissolving 10 mg of vardenafil hydrochloride in 1000 ml of distilled water in calibrated flask.

Estimation of absorption maxima
The standard solution of vardenafil hydrochloride (1µg/ml) was scanned in the range of 200-400nm which show maxima located at 214 (Figure 2). The higher absorption value at 214 nm results in increasing sensitivity of the method at this maximum. Therefore, 214 nm wavelength was selected for the construction of calibration curve.

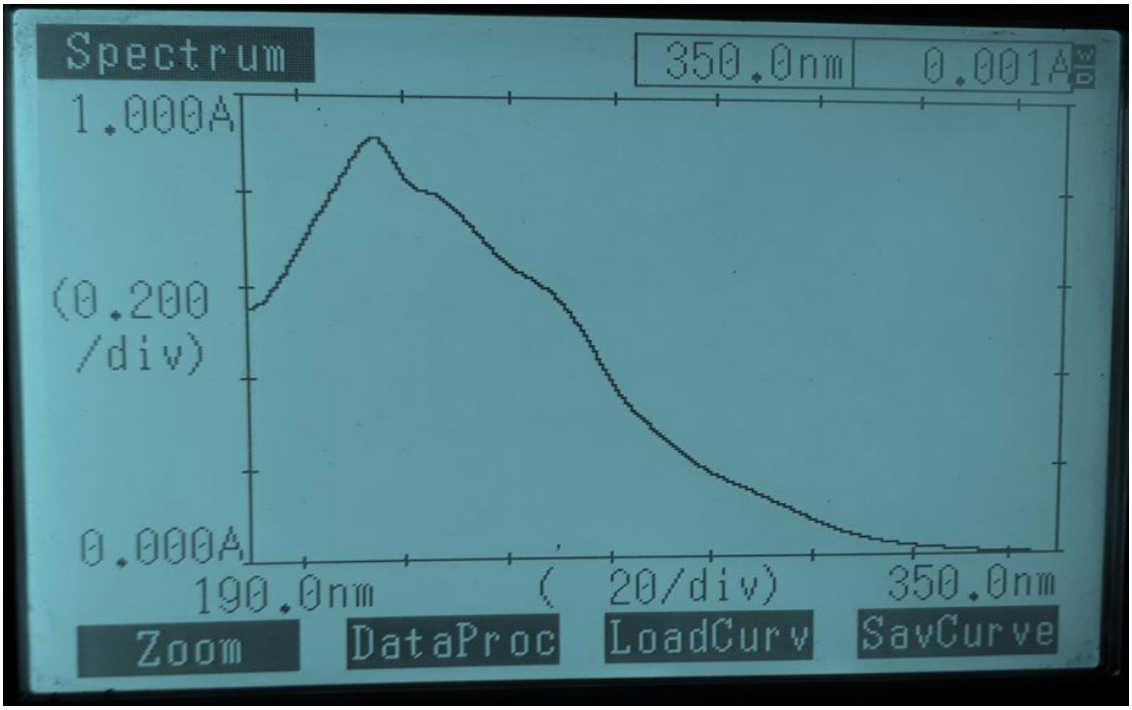


Figure 2: Absorption spectra of 1µg/ml vardenafil hydrochloride against distilled water.

Recommended procedure
From the absorption maxima, calibration curve was prepared in the concentration range of 0.1-2 µg/ml. The absorbance was measured at 214 nm against distilled water as a blank. The concentration of the sample solution can be determined by using the calibration curve.

Procedures for pharmaceutical preparations
To minimize a possible variation in the composition of the tablets (containing 20mg of Vardenafil hydrochloride tablet were provided from(PIONER), company for pharmaceutical industries –Iraq. The mixed content of 4 tablets were weighed and grounded, then the powder equivalent to 1.0 mg of Vardenafil hydrochloride in about 70 ml of distilled water was stirred well for 30 min and then filtered through whatman No. 42 filter paper and the filtrate solution was diluted to 100ml by distilled water and different volume of this solution was treated as described above under general procedure. and the concentration was calculated by using the calibration curve of this method.

Procedure for real water samples
To demonstrate the practical applicability of the proposed method, real water samples were analyzed by this method. Industrial waste water from the state company for drug industries and medical appliances Mosul-Iraq, were fortified with the concentrations in the range of 0.2,0.8,1.6 µg/ml of vardenafil hydrochloride. The fortified water samples were analyzed as described above for recommended procedure and the concentration was calculated by using the calibration curve of this method.

RESULT AND DISCUSSION
UV- Visible spectrophotometry is still considered to be a convenient and low cost method for the estimation of pharmaceuticals.[17-20] This method used for the estimation of vardenafil hydrochloride in pharmaceutical preparations and environmental wastewater samples was found to be high sensitive, simple, accurate, and reproducible. Beer s law was obeyed in the concentration range of 0.1-2 µg/ml (Figure 3) with correlation coefficient of 0.9996, intercept of 0.0003 and slope of 0.9037 The conditional molar absorptivity was found to be 4.745×10^5 $L.mol^{-1}.cm^{-1}$ and sandell's sensitivity was

1.107ng.cm^{-2}. The limit of detection and quantification were evaluated as:
LOD = Intercept /Slopex10
And LOQ = 3.3LOD

The limit of detection was 3.32ng/ml and the limit of quantification 10.96ng/ml as the lowest standard concentration which could be determine with acceptable accuracy.

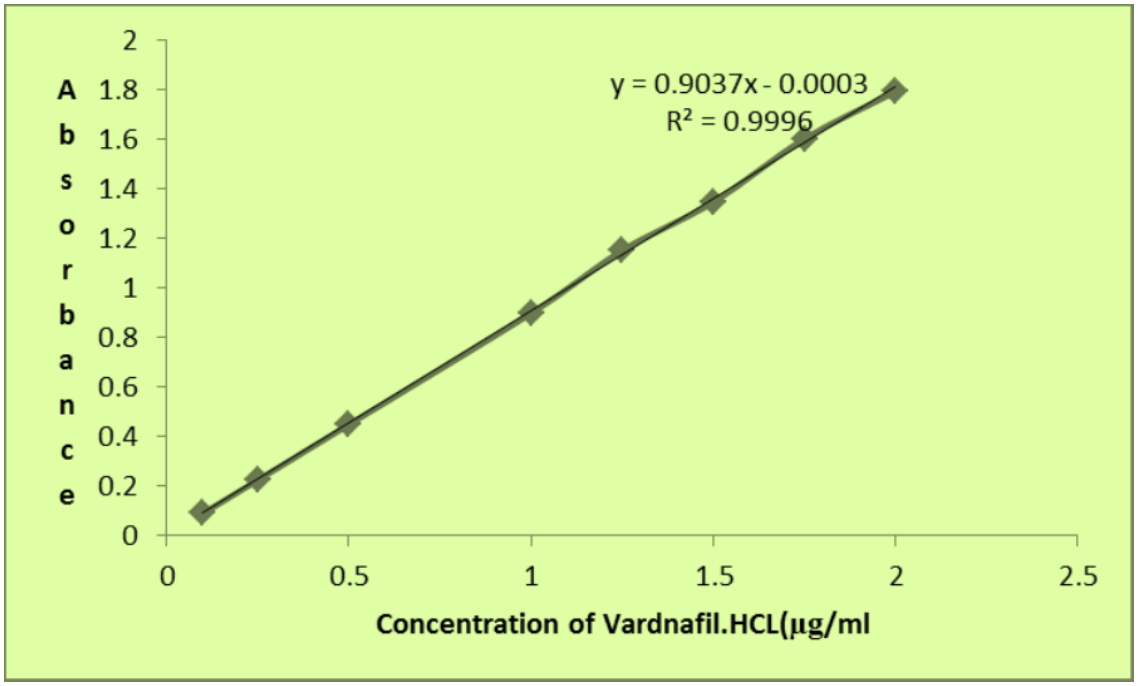


Figure 3: Calibration graph of vardenafil hydrochloride.

The accuracy and precision of the method, a pure drug solution was analyzed at three different concentrations, each estimation being repeated six times. The relative error(%) and relative standard deviation values are summarized in (table 1). From table 1 the values of standard deviation were satisfactory and the recovery studies were close to 100%,. The RSD% value is less than 2 indicative of accuracy of the method.

Table (1): Accuracy and precision of the proposed method.

(Vardenafil hydrochloride taken µg/ml)	Er (%)[a]	RSD(%)
0.2	1.01	1.3
0.8	1.02	1.6
1.6	1.02	1.4

a: Mean of six estimations.

Interference studies

In order to assess the possible applications of the proposed method, the effect of substance that often accompany with vardenafil hydrochloride in (Tablets) were studied by adding different amount of substances to 1 µg of vardenafil hydrochloride An attractive feather of the method is its relative freedom from interference by the usual diluents and excipients in amounts for in excess of their normal occurrence in pharmaceutical preparations. The results are given in (table 2).

Table (2): Estimation of 1 µg of vardenafil hydrochloride in the presence of excipients and other substances.

Interfering substances	Amount added/mg of interfering	Amount of drug found*µg	RSD %
Lactose	40	1.01	0.61
Microcrystalline cellulose	20	1.06	0.64
Corn starch	30	1.07	0.77
Povidone	30	1.05	0.78
Magnesium stearate	40	1.07	0.94
Hydroxyl propyl methyl cellulose	40	1.07	0.96
Poly ethylene glycol	20	1.01	0.95
Titanium dioxide	10	1.05	0.89

*Average of six estimations.

Analytical application

The proposed method was satisfactorily applied to the estimation of vardenafil hydrochloride in its pharmaceutical preparations tablets and wastewater samples, the results of the assay of the pharmaceutical preparations revels that there is close agreement between the results obtained by the proposed method and the label claim (Table 3), and the results of water samples (Table 4) show that the recovery values obtained were closed to 100%.

Table (3): Estimation of vardenafil hydrochloride in pharmaceutical formulation.

Pharmaceutical formulations supplied by PIONER Tablets	Label amount (mg/tab)	Found by proposed method (mg) *	Recovery%
Horse man tablet 20mg	20mg/tab	19.96	100.2

*mean value of ten estimations.

Table (4): Estimation of vardenafil hydrochloride in wastewater samples.

Wastewater samples	Added µg/ml	Found* (µg/ml)	Recovery %(n=10)
Industrial wastewater	0.2	0.202	101
	0.8	0.802	100.25
	1.6	1.606	100.375

*mean value of ten estimations.

Application of the proposed method to content uniformity[21,22]

Content uniformity or the Uniformity of dosage unit was defined as the degree of uniformity in the amount of active substance among dosage units. The risk assessment strategy underlying content uniformity testing is the assumption that some pre-specified limits exist where safety and efficacy outcomes may change if content uniformity fails. The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in (table 5) indicate that the proposed method cans accurately and precisely quantitative Vardenafil hydrochloride in its commercially available tablets. The mean percentage (with RSD) of the labeled claim found in ten tablets was 100.09(0.663%) which fall within the content uniformity limits specified by the Japanese Pharmacopoeia.[21]

Table (5): Content uniformity testing of Vardenafil hydrochloride tablets using the Proposed method.

Parameter	% of the label claim
Tablet No.1	100.3
Tablet No.2	99.9
Tablet No.3	100.6
Tablet No.4	100.2
Tablet No.5	99.6
Tablet No.6	100.1
Tablet No.7	99.8
Tablet No.8	100.2
Tablet No.9	100.4
Tablet N0.10	99.8
Mean(X)	100.09
%RSD	0.663
Max. allowed unit value[21]	±15%

CONCLUSIONS

The applied method was found to be ultra-sensitive, simple, rapid, accurate, precise, and low economical cost. Furthermore, the proposed method doesn't require elaboration of procedures, which are usually associated with chromatographic methods. The proposed method could be applied successfully for determination of Vardenafil Hydrochloride in environmental water samples, and pharmaceutical pure form as well as in tablet dosage forms.

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