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NEW METHOD DEVELOPMENT AND VALIDATION OF TADALIFIL USING UV- VISIBLE SPECTROPHOTOMETR

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ABSTRACT

Three simple, economical, precise and reproducible visible spectrophotmetric methods have been developed for the estimation of Tadalifil in bulk formulation. The developed methods are based on the formation of charge transfer coloured complex of Tadalifil with N-Bromo succinimide, complexes with chloramine-T and phosphymolybdic acid using double distilled water. The complexes with N-Bromo succinimide, chloramine-T and phosphymolybdic acid shows absorbances maxima at 520.0 nm, 540.0 nm 840.0nm and linearity in the concentration range of 1-20 µg/ml, 0.5-1.0 µg/ml and 10-30 µg/ml . Results of analysis for all the three methods were validated statistically and by recovery studies. The molar absorpitivity, Sandell sensitivity, Corelation coffecient were also calculated.

Key words: UV-Visible Spectrophotometry, Tadalifil, Ultra Sonicator, Electronic balance, Millipore double distilled water, N-Bromosuccinimide, Chloramine-T, Gallocyanine and Phosphymolybdic acid.

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INTRODUCTION

Tadalifil (TDF) is apotent and selective, reversible inhibitor of cyclic guanosine mono phosphate (CGMP) specific phoshpo diesterase type 5(PDE) inhibitor used in the management of erectile dysnfunction It is not official in any of the pharmacopoeias. On treatment with different strengths of base, acid and hydrogen peroxide the degradation was observed with high standards.It is a secondary messenger for the smooth muscle relaxing effects of nitric oxide, which plays an important role in the vasodilation of erectile tissues.[1-2]

The chemical name of tadalafil is (6R-trans)-6-(1,3- benzodioxol-5-yl)-2,3,6,7,12,12a-hexa hydro-2-methyl-pyrazino[1',2':1,6.]pyrido[3,4-b]indole 1,4-dione and it's empirical formula is $C_{22}H_{19}N_3O_4$. The structure is

Literature survey reveals few HPLC methods, few UV and visible methods[3-11] have been developed for estimation of tadalifil in tablet and pure form.

Objective:

The objective of the present investigation is to develop simple, accurate and economical visible spectrophotometric methods for quantization of tadalifil in bulk formulation.

EXPERIMENTATION

Materials and Methods

Instrumentation: ELICO UV 177, UV/Vis Spectrophotometer wavelength accuracy of ± 0.3 nm and 1.0 cm matched quartz cells was used for analytical method development.

Preparation of stock solution and experimental solution:

Standard solution of Tadalifil was prepared by dissolving 50 mg in 50 ml of methanol and diluting 10 mLof this solution to 100 mL with ethanol (100µg/mL). 50 mg of pure Ttadalifil is transferred into a 50 mL volumetric flask containing 20 mL of methanol and flask was kept for ultrasonication for 4-5 min,

then it is diluted up to the mark with methanol solution. From the above solution 5ml and 10 mL are pipetted out into a 100 mL volumetric flask separately and the volumes are made up to the mark with methanol. These final concentrations of Tadalifil are used for the analysis of method1, method2 and method3 respectively.

Method I:

In the first method aliquots of Tadalifil ranging from 0.5-5 mL of standard solution of 100ppm are transferred to each 25 mL calibrated tubes, 0.5 mL of 5% w/v acetic acid and 2ml of 0.1% N-Bromosuccinimide standardized iodometrically solutions were added to the above solutions and volume in each tube was brought to 10ml with double distilled water and kept aside for 20minutes at room temoperature. Then 2ml of 0.3% metol (p-N-methyl aminophenol sulphate) solution was added. After 2minutes, 2ml of 0.2% sulphanilamide(SA) solution was added and volume was made upto the mark with double distilled water. The absorbance's are measured after 10minutes at 520nm against double distilled water. A blank experiment was also carried out by omitting the drug. The decrease in absorbance and in turn the drug concentration was obtained by subtracting the absorbance of the test solution from the blank. The calibration graph was drawn by plotting the decrease in the absorbance.

The proposed reaction for the method-I is

Drug+ excess NBS Succinimide+NBS (unreacted)+ oxidation products of drug

NBS (unreacted) + PMAP (metol) 2PMBQMI

PMBQMI +SA charge transfer complex

Method II:

In the second method aliquots of Tadalifil(TDF) ranging from 0.1ml- 0.4mL of 50 ppm standard solution is transferred in to a series of graduated tubes, 1.25ml of 5M HCl and 2.0ml of 0.02% Chloramine-T(CAT) standardized iodometrically were added and the bsolution was diluted to 20ml with double distilled water. After 10minutes, 5ml of 0.01% Gallocyanine(GC) was added mixed thoroughly and the absorbance's are measured after 15minutes at 540nm against double distilled water. A blank experiment was also carried out in a similar manner. The decrease in absorbance corresponding to consumed chloramines-T, which in turn the drug concentration was obtained by subtracting the absorbance of the blank solution from that of the test solution. The calibration graph was drawn by plotting the decrease in the absorbance of the dye against amount of the drug.

The proposed reaction for the method-II is

(TDF)Drug + CAT (excess) → Oxidation products of drug + un reacted CAT

CAT (unreacted) +GC → unreacted dye GC coloured + mixture of compounds

Method III:

To the standard drug solution of Tadalifil (0.25ml-1.0ml, 100ppm) taken in a 25ml volumetric flasks,0.5 mL of 2% PMA was added and waited for 10mts. The precipitate obtained is dissolved in 5 mL of acetone. To that 0.5mL of 2% EDTA and 0.5mL of 1% $Co(NO_3)_2$ are added and heated for 10 minutes. Then cooled to room temperature and volume is made upto 25 mL with double distilled water. The optical density was measured at 840 nm against a similar reagent blank. The amount of the drug Tadalifil present was deduced from the calibration curve. A molecular complex results by the interaction of unshared electron on nitrogen in heterocyclic moiety of drug and unoccupied molecular orbital of heteropoly acid molecule.

Recovery Studies

The recovery was in the range of 99-100 % for all the three methods. High percentage of recovery shows the method is free from interference of excipients present in pure form.

RESULTS AND DISCUSSION

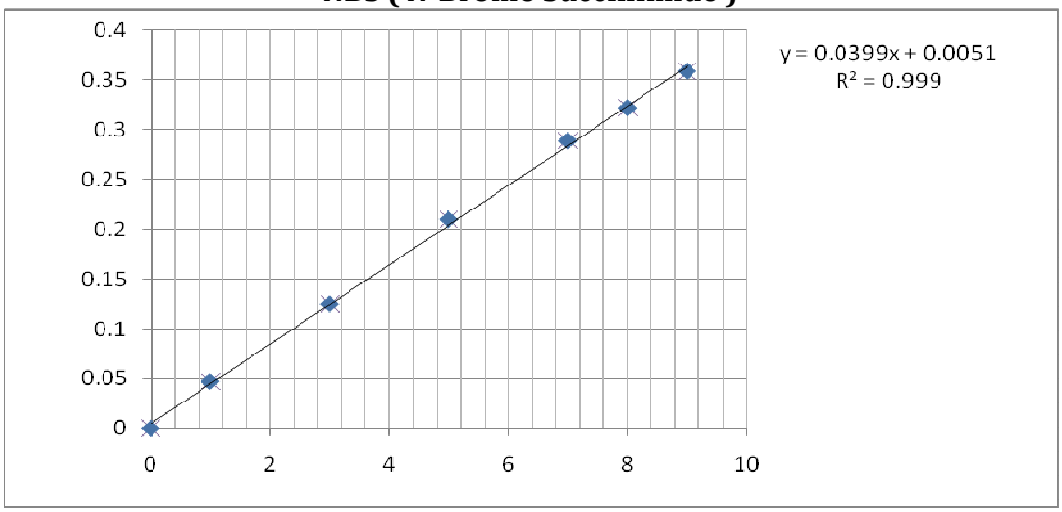
The proposed methods for the Tadalifil drug by visible spectro photometer are simple, accurate, economical and superior. The methods developed obeys Beer's law in the concentration range of 1-20 µg/ml with N-Bromosuccinimide, 0.5-1.0µg/ml with Chloramine-T and 10-30µg/ml with phosphymolybdic acid. The proposed methods gave results with good accuracy to permit determination of low concentrations. Validation for the above methods was done and the parameters are tabulated in tabular form and also in graphical representation by taking concentration in X-axis and Absorbance in Y-axis. The recovery studies were carried out by standard addition method and were found close to 100 %. The wide applicability of the described procedure for routine quality control is well established by the TDF in pure form.

Table: Optical Characteristics of Tadalifil (TDF)

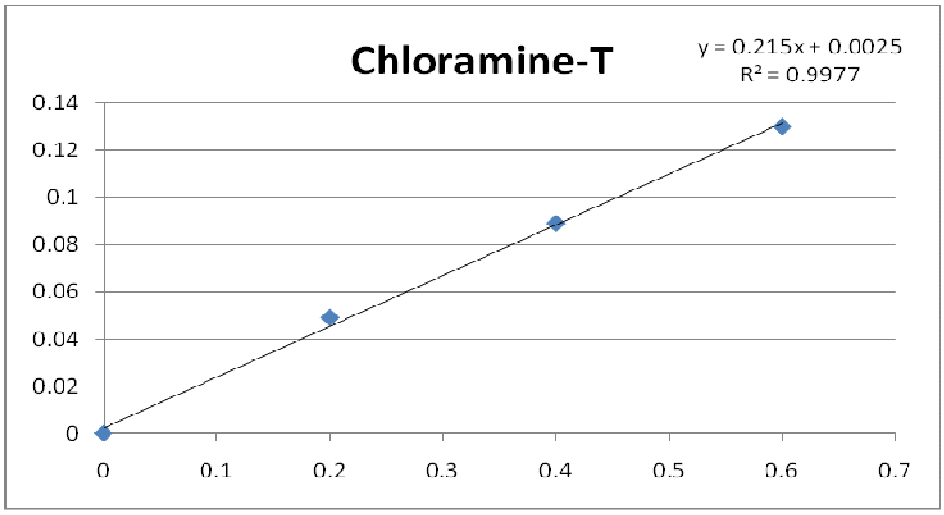
PARAMETERS	METHOD I	METHOD II	METHOD III
λ max	520.0 nm	540.0 nm	840.0 nm
Beer's law limit (µg/ml)	1-20	0.5-1.0	10-30
Regression equation* (y = a + bc)	y = 0.0331x - 0.0103	y = 0.215x + 0.0025	y = 0.0037x - 0.0009
Slope (b)	0.0331	0.215	0.0037
Intercept (a)	- 0.0103	0.0025	- 0.0009
Correlation coefficient (r^2)	0.999	0.9977	0.999
Molar Absorptivity	$1.23X10^4$	$8.47X10^4$	$1.42X10^4$
Sandell's Senstivity (g/cm^2/ 0.001 abs unit)	3.16 X 10^{-2}	4.6 X 10^{-3}	2.74 X 10^{-1}

* y = a + bc, where c is the concentration in µg/ml, y is the absorbance unit of four replicate samples and b is the slope of line equation.

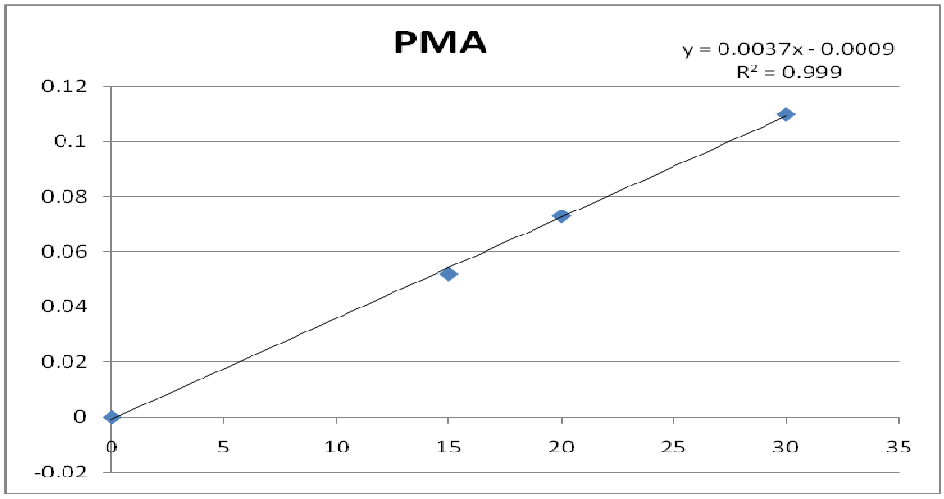
Spectral characteristics of Tadalifil (TDF)
NBS (N-Bromo Succinimide)



Chloramine-T



(PMA)Phosphy Molybdic Acid



CONCLUSION

Thus it can be concluded that the methods developed in the present investigation are simple, sensitive, accurate, rapid and precise. Hence, the above said methods can be successfully utilized for the estimation of tadalafil in pure form.

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