Int J Pharm Bio Sci 2016 April; 7(2): (P) 254 - 264

Original Research Article **Pharmaceutics**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

SPECTROPHOTOMETRIC DETERMINATION OF DRUGS AND PHARMACEUTICALS USING $KMNO_4$ AS OXIDANT AND METHYL ORANGE DYE AS ANALYTICAL REAGENT

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ABSTRACT

Simple, sensitive and accurate methods for spectrophotometric determination of five drugs *viz.,* Atrovastatin Calcium, Rosuvastatin Calcium, Sildenafil Citrate, Verapamil Hydrochloride and Amlodopine Besylate has been developed. These methods depend upon the oxidation of the drug by a known excess $KMnO_4$ in sulphuric acid medium and subsequent determination of unreacted $KMnO_4$ with Methyl Orange dye and measuring the absorbance at 507nm. These methods have been validated in terms of LOD, LOQ, precision accuracy, %RSD, robustness and ruggedness. Factors affecting the absorbance *viz.,* concentration of H_2SO_4 and time of reaction are optimized. The effect of excipients has also been studied and found to have no effect. The calibration curves are found useful for determination of pure drug and can be applied to pharmaceuticals in bulk drug and pharmaceutical industries.

KEYWORDS: **Spectrophotometry, Drugs, $KMnO_4$, Methyl Orange dye, Validation.**

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INTRODUCTION

Atorvastatin Calcium (ATV) is a synthetic lipid-lowering agent. It is chemically known as [R-(R*,R*)]-2-(4-fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino) carbonyl]-1H-pyrrole-1-heptanoic acid calcium salt (2:1) trihydrate [Fig I] belongs to the group of statins.[1,2] All Statins including ATV reduce the production of cholesterol in the liver. ATV is a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor is a lipid regulating drug used to reduce LDL-cholesterol, apolipoprotein B and triglycerides and to increase HDL-cholesterol in the treatment of hyperlipidaemias. It is also used for prophylaxis of regulating drug used to reduce LDL-cholesterol, apolipoprotein B and triglycerides and to increase HDL-cholesterol in the treatment of hyperlipidaemias. It is also used for prophylaxis of cardiovascular events in patients with multiple risk factors including diabetes mellitus. Several methods have been reported for quantitative determination of ATV in HPTLC[3-5], RP-HPLC[6-8], HPLC[9-11] and Spectrophotometric method[12] for bulk drug and Tablets. Rosuvastatin Calcium (ROSU) is a synthetic lipid lowering agent which is used in hypercholesterolemia and dyslipidemia.[13] It inhibits the enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate limiting enzyme that converts HMGCoA to mevalonate a precursor of cholesterol and thereby checks the synthesis of cholesterol.[14] It is chemically known as bis [(E)-7 [4-(4-fluorophenyl)-6 isopropyl- 2-[methyl (methyl-sulphonyl) amino] pyrimidin-5-yl] (3R, 5S) -3,5 dihydroxyhept-6-enoicacid] Calcium salt.[1,2] A survey of literature showed few LC–MS/MS with electrospray ionization method[15-17], UV spectrophotometric [18-21], HPLC [22-25], RP- HPLC[26,27], HPTLC[28] and Voltammetry[29] methods are available for the estimation of Rosuvastatin in pharmaceutical preparation and in biological fluids. Sildenafil Citrate (SDC) was patented in1996 and launched in May 1998 as first oral drug approved by Food and Drug Administration (FDA) to treat erectile dysfunction (ED) in the United States. It is also effective for treatment of pulmonary arterial hypertension (PAH). It is a popular drug marketed as Viagra by Pfizer. Sildenafil Citrate (SDC) is designated chemically as 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazole [4,3-d] pyromidine-+5-yl)-4-ethoxyphenyl] sulfonyl]-4-methylpiperazine Citrate. The mechanism of action of Sildenafil involves the protection of cyclic guanosine monophosphate (cGMP) from degradation by cGMP – specific phosphodiesterase type5 (PDE5) in the corpus cavernosum. Nitric oxide (NO) in the corpus cavernosum of the penis binds to guanylate cyclase receptors which results in increased levels of cGMP leading to smooth muscle relaxation (vasodilation). This smooth muscle relaxation leads to vasodilation and increased inflow of blood into the spongy tissue of the penis causing an erection.[30,31] It is eliminated predominantly by hepatic metabolism and converted to an active metabolite with properties similar to the parent Sildenafil. Sildenafil may be useful for the prevention and treatment of high-altitude pulmonary edema associated with altitude sickness such as that suffered by mountain climbers.[32] ¨Literature survey reveals that there are some reported analytical methods like Voltammetry[33], RP-LC method[34], Atomic absorption spectrometric method,[35] UV spectroscopy[36,37], HPLC[38-40] methods are reported for estimation of Sildenafil Citrate in bulk drug, formulations, pure active pharmaceutical ingredient and tablet dosage.

Verapamil Hydrochloride (VPM) is chemically known as (±)-5-[N-(3,4- dimethoxyphenethyl) methylamino]-2-(3,4-dimethoxyphenyl)-2-isopropylvaleronitrile monohydrochloride. It is clinically a very useful member of an L-type calcium channel blocker of the phenylalkylamine class. The drug reduces systemic vascular resistance & mean blood pressure, with minor effect on cardiac output. It is used in the treatment of supraventricular arrhythmias, angina pectoris, migraine, hypertension[41,42] and most recently cluster headaches.[43] Verapamil has also been used as a vasodilator during cryopreservation of blood vessels. Literature survey revealed that several methods have been reported for quantitative determination of VPM in HPLC[44], RP-HPLC[45], LC-MS[46] and Spectrophotometric method[47,48] for bulk drug and Tablets. Amlodipine Besylate is chemically known as 2-[(2-aminoethoxy)-methyl]-4-2-chlorophenyl), 1,4-dihydro-6-methyl-3,5-pyridine dicarboxylic acid and 3-ethyl-5-methyl ester. It is a potent long-acting dihydropyridine calcium-channel blocker that inhibits the trans membrane influx of calcium ions into vascular smooth muscles and cardiac muscles which in turn affects their contractile process and results in reduced blood pressure. It is the besylate salt of amlodipine. It is used in the treatment of hypertension and angina.[1] Literature survey reveals that there were some reported analytical methods like HPTLC[49], HPLC[50-51], Stability indicating LC method[52], RP-HPLC[53], Spectrophotometric methods[54-57] are reported for estimation of Amlodipine Besylate in bulk drug, formulations, pure active pharmaceutical ingredient and tablet dosage. Although much work has been published on the quantification of the above drugs but the simplest method using oxidative spectrophotometry has not been reported yet. In the present communication we report the oxidation of drug by $KMnO_4$ – Methyl Orange dye couple to report the quantification of drug by $KMnO_4$ as oxidant and Methyl Orange dye as analytical reagent.

Structure of drugs

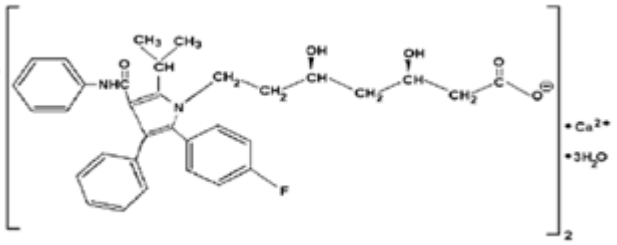

Figure I
Atorvastatin Calcium

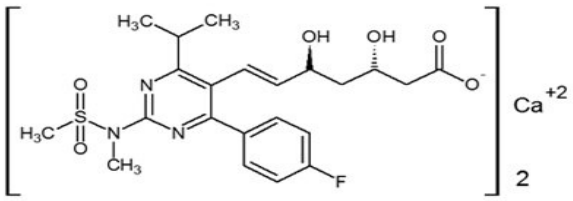

Figure II
Rosuvastatin Calcium

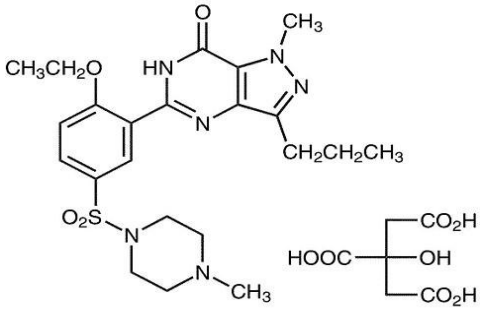

Figure III
Sildenafil Citrate

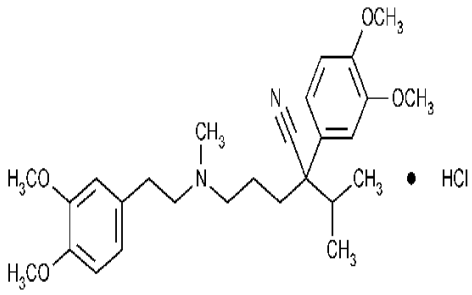

Figure IV
Verpamil

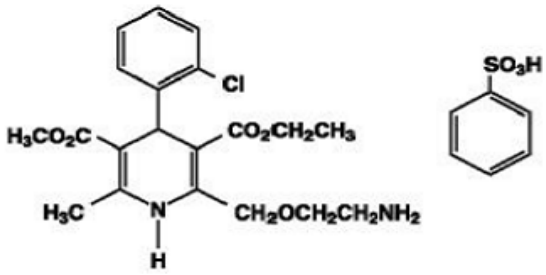

Figure V
Amlodipine Besylate

Thorough literature survey on the above mentioned drugs revealed that quantification using $KMnO_4$ as oxidizing agent has not been reported yet although the reagent is cheap, common and gives simple, sensitive, accurate method of quantification for drugs.[58-60] This prompted the authors to develop an oxidative spectrophotometric method for the above cited drugs by using $KMnO_4$ as oxidizing agent and Methyl Orange dye as analytical reagent. This spectrophotometric method involved the addition of excess $KMnO_4$ in acidic medium to the drug and un reacted $KMnO_4$ is estimated by Methyl Orange dye which is readily oxidizable by $KMnO_4$ and found suitable for estimation of unreacted $KMnO_4$ at 507 nm absorbance.

MATERIALS AND METHODS

Instrumentation

The UV-VIS spectra of the study have been recorded on ELICO 210 double beam spectrophotometer, Thermo Nicolet 1000 and also on ELICO 159 UV-VIS single beam spectrophotometers using quartz cells of 10 mm path length. A Dhona 200 single pan electrical balance is used for weighing the samples. All reagents used were of analytical-reagent grade and distilled water was used throughout the investigation. $KMnO_4$ Stock Solution (0.001 mol L^{-1}) was prepared by dissolving 0.0158gm of Potassium Permanganate ($KMnO_4$) (S.D. Fine CHEM Limited, Mumbai, India) in 100mL standard flask with double distilled water. The $KMnO_4$ stock solution was then diluted to get working concentrations of 63.2µg mL^{-1} A stock solution of Methyl Orange dye (160µg mL^{-1}) was prepared by dissolving an appropriate weight of dye (Himedia Laboratories Pvt, Limited) in double distilled water. The Methyl Orange stock solution was then diluted to get working concentrations of 80µg mL^{-1}. Sulphuric acid was prepared by diluting the concentrated acid (Merck, Mumbai, India, Sp. gr. 1.84, 98.0 %) with distilled water appropriately to get 2*M* acid solution. Standard drug solution (200 µg mL^{-1}) was prepared by dissolving accurately weighed 20 mg drug with a suitable solvent to the mark in 100 mL standard flask. The stock solutions of ATV, ROSU, SDC, VPM and ADB were further diluted with the same solvent to obtain working concentrations.

Assay Procedure

Aliquots containing 1.5-10.5 µg mL^{-1} (ATV), 3.2-22.4 µg mL^{-1} (ROSU), 1.0-7.0 µg mL^{-1} (SDC), 1.4-9.8 µg mL^{-1} (VPM) and 3.4-23.8 µg mL^{-1} (ADB) of drug were transferred into a series of 10 ml standard flasks using a micro burette. To this, 1 mL of $KMnO_4$ was added followed by 1 mL of 2*M* H_2SO_4 and contents were shaken well. After 15 minutes, 1mL of 80µg mL^{-1} of Methyl Orange solution was added to the contents. Then contents were shaken well and diluted with double distilled water up to the mark. The absorbance of each solution was measured at 507 nm against the corresponding reagent blank. To test the accuracy and precision of the methods developed, pure sample solutions containing drug in the Beer's Law limit were chosen. For this study 1.5-10.5 µg mL^{-1} of ATV, 3.2-22.4 µg mL^{-1} of ROSU, 1.0-7.0 µg mL^{-1} of SDC, 1.4-9.8 µg mL^{-1} of VPM and 3.4-23.8 µg mL^{-1} of ADB. To each of the solution 1 mL of 63.2 µg mL^{-1} of $KMnO_4$, 1 mL of 2*M* of H_2SO_4 were added and the un reacted $KMnO_4$ is analyzed as described above using Methyl Orange dye. Calibration curves were constructed for all the drugs by plotting the absorbance versus the concentration of drugs. The absorbance data were collected for six replicate experiments and absorbance to concentration ratio called the relative response was determined. The relative responses from 95% to 105% of average are only considered for construction of the Calibration curve.

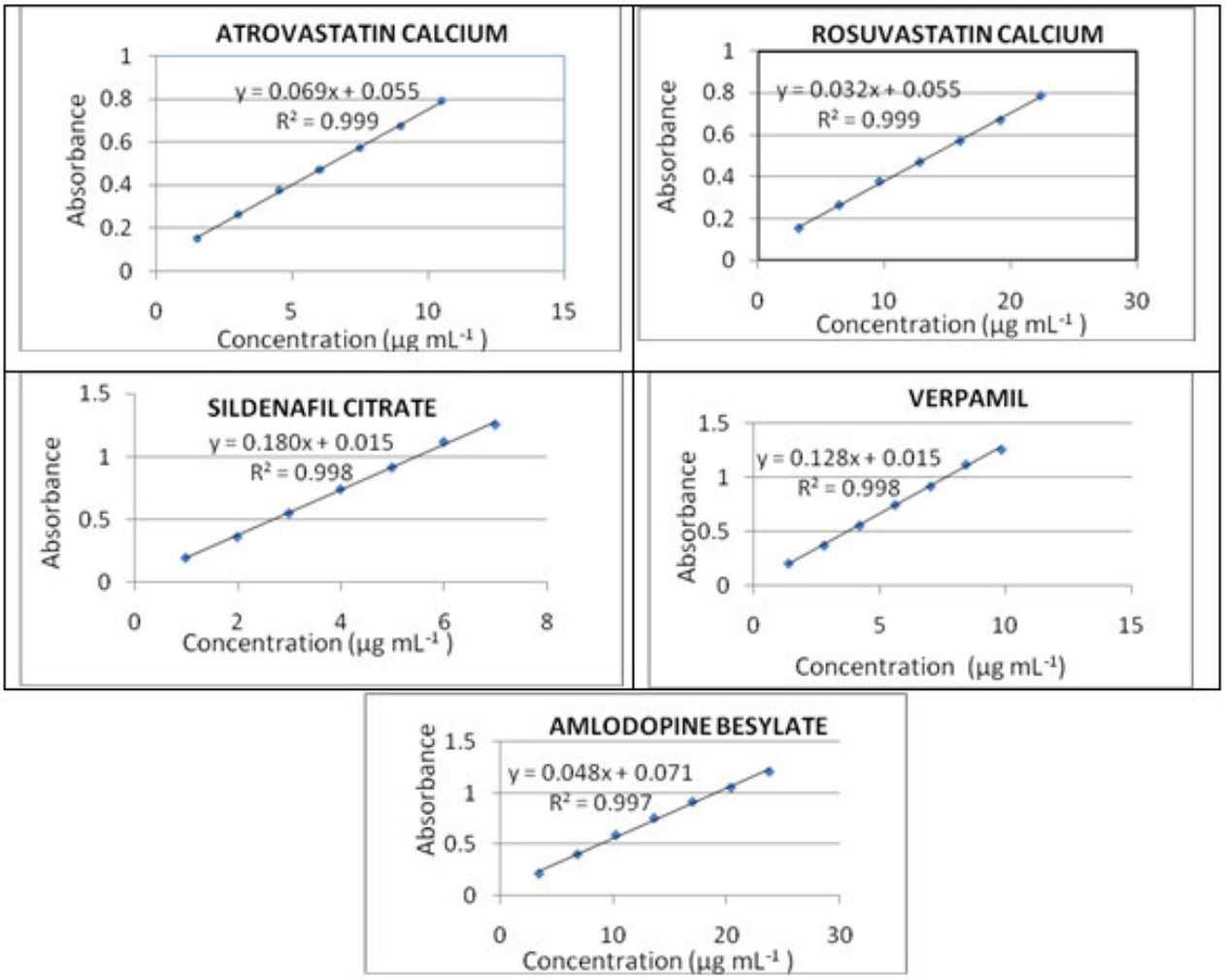

Figure 6
Calibration curves of drugs - ATV, ROSU, SDC, VPM and ADB.

Procedure for assay of pure drug
Sample solutions of each drug in the beer's law limits were chosen and recovery experiments were performed to check the accuracy and precision. The concentration chosen and % of recovery are tabulated in table2, for this purpose standard deviation method also adapted. Excellent recovery and %RSD being less than 2 speaks about the precision and accuracy of the method.

Procedure for tablets
Atrovastatin calcium
Two tablets (ATROVASTATIN CALCIUM-10mg) were crushed to a fine powder and the powder equivalent to 10 mg of Atrovastatin Calcium was weighed accurately, transferred into a 100 mL calibrated flask, dissolved in sufficient quantity of methanol, sonicated for 10 min and the volume was finally diluted to the mark with methanol. This solution was mixed well and filtered through Whatman filter paper No. 42. It was used as stock sample solution and was further diluted with the same solvent to get working standard solution.

Rosuvastatin Calcium
Two tablets (Rosuvas-20mg) were crushed to a fine powder and the powder equivalent to 10 mg of Rosuvastatin Calcium was weighed accurately, transferred into a 100 mL calibrated flask, dissolved in sufficient quantity of methanol, sonicated for 10 min and the volume was finally diluted to the mark with methanol. This solution was mixed well and filtered through Whatman filter paper No. 42. It was used as stock sample solution and was further diluted with the same solvent to get working standard solution.

Sildenafil Citrate
One tablet (Sildenafil Tablets, VEGRO-100mg) were weighed accurately, crushed to a fine powder, the powder equivalent to 10mg of Sildenafil Citrate was weighed accurately, transferred to 100mL volumetric flask, dissolved in sufficient quantity of methanol, sonicated for 10 minutes and the volume was finally diluted to the mark with methanol. This solution was mixed well and filtered through Whatman filter paper No. 42. It was used as stock sample solution and was further diluted with the same solvent to get working standard solution.

Verpamil
Two tablets (Vasopten -40mg) were crushed to a fine powder and the powder equivalent to 10mg of Verpamil was weighed accurately and transferred to 100 mL volumetric flask, dissolved in sufficient quantity of methanol, sonicated for 10 minutes and the volume was finally diluted to the mark with methanol. This solution was mixed well and filtered through Whatman filter paper No. 42. It was used as stock sample solution and was

further diluted with the same solvent to get working standard solution.

Amlodopine Besylate

Ten tablets **(** NORVASC (Pfizer Inc), 2.5mg) were crushed to a fine powder. A quantity equivalent to10 mg of Amlodopine Besylate was weighed accurately, transferred into a 100 mL calibrated flask and the volume was finally diluted to the mark with double distilled water, mixed well and filtered using a Whatman No. 42 filter paper. It was used as stock sample solution and was further diluted with water to get working standard solution.

Method of validation

The each method developed for quantification of drugs has been validated in terms of precision, accuracy, limit of detection, limit of quantification, linearity, selectivity and ruggedness. Absorbance-concentration curves were drawn, the fixed time method was used to assess the recovery of the drug. To assess the precision each experiment was repeated at least 6 times and accuracy is estimated in terms of percent recovery and percent RSD. Excellent percent recovery and RSD being less than 2 for each drug demonstrates accuracy and precision of the methods.[Table2]. As mentioned earlier limit of detection is the minimum limit that can be detected but not necessarily quantified is determined for each drug. LOD is determined from the standard deviation of y-intercepts of regression lines of replicate determinations.

LOD = 3.3 s_a/S

Where s_a = standard deviation of intercept (n=6)

S = slope of linearity plot

LOQ the minimum concentration of analyst using calibration curve is also determined.

LOQ = 10s_a/S.

Limits of linearity of calibration curves [Fig. 6] are mentioned under the title Beer's law limit. To test the selectivity known excipients of each drug are added to the pure drug sample and recovery experiments were performed. Ruggedness is resistance of method for a small change in variables like instrument and analyst or both to test the ruggedness of the method. Absorbance data was collected using 3 different instrument and 2 analysts. No significant changes were observed either by change of instrument or analyst hence the method may be taken as robust.

Factors effecting absorbance and selection of acid

To study the effect of acid, different types of acids were examined (H_2SO_4, H_3PO_4 and CH_3COOH) to achieve maximum yield of Redox reaction. The results indicated that the Sulphuric acid was the preferable acid with $KMnO_4$ as oxidant. To study the effect of acid concentration, different concentrations of H_2SO_4 were examined. The reaction was performed in a series of 10 ml volumetric flask containing 12.0 µg mL^{-1} of the cited drugs, different volumes (0.5–2.5 mL) of 0.5*M* , 1.0*M* , 1.5*M* ,2.0*M, 2.5M* H_2SO_4 and 1 mL of $KMnO_4$ (63.2µg mL^{-1}) were added. After 15 min of time, 1.0 mL of Methyl Orange dye (80 µg mL^{-1}) and water added upto the mark. It was found that the maximum absorbance was obtained with 1mL of 2*M* H_2SO_4. Above this volume, the absorbance decreased therefore a volume of 1 mL of 2*M* H_2SO_4 was used for all measurements. In order to obtain the highest and most stable absorbance, the effect of time on the oxidation reaction of drugs were catalyzed by the time periods ranging for 2.5-20 minutes, the time required to complete the reaction and maximum absorbance was obtained after 15 minutes.

Analysis of pharmaceuticals

To the test the applicability of the method developed solution of pharmaceutical tablets solutions containing drug in the Beer's Law limit were chosen. To assess the precision each tablet analysis was repeated at least 6 times and accuracy is estimated in terms of percent recovery and percent RSD. Excellent percent recovery and RSD being less than 2 for each drug demonstrates applicability of the methods for pharmaceutical analysis [Table III]. The excellent recovery studies indicate that methods developed can be applied to pharmaceutical analysis without hesitation.

RESULTS AND DISCUSSION

The ability of $KMnO_4$ to oxidize drugs and bleach the color of Methyl Orange dye is the basis of the indirect spectrophotometric method developed here. In this method the drugs were reacted with a measured excess of $KMnO_4$ in acidic medium and the unreacted oxidant was determined by reacting with Methyl Orange followed by absorbance measurement at 507 nm (scheme1). The absorbance increased linearly with increasing concentration of drug, when increasing amounts of each drug were added to a fixed amount of 63.2 µg mL^{-1} of $KMnO_4$, consumed the latter and there occurred a concomitant fall in its concentration. When fixed amount of the dye was added to decreasing amount of oxidant, a concomitant increase in the concentration of dye resulted. This was observed as a proportional increase in absorbance at the respective λ_{max} with increasing concentration of each drug. One ml of 2*M* acid was used in the reaction, as this concentration was found ideal.

Drug + $KMnO_4$ excess → Drug oxidation product +$Mn^{+2/+4}$ + $KMnO_4$ unreacted;

$KMnO_4$ unreacted + Methyl Orange → oxidation product of Methyl Orange + Unreacted Methyl Orange, measured spectrophotometrically at λ_{max} = 507 nm.

Tentative reaction scheme for the indirect determination of drug by oxidation with $KMnO_4$

Analytical data

A linear correlation was found between absorbance at λ_{max} and concentration ranges, and sensitivity parameters such as Sandal's sensitivity, detection limit and quantification limit calculated according to ICH guidelines[61] are also presented in table I and reveal the very high sensitivity of the methods. Regression analysis of Beer's law data using the method of least squares was made to evaluate the slope (b), intercept (a), correlation coefficient (r) and is also given in [Table I].

Table I
Analytical and Regression parameters of Spectrophotometric Method

Name of drug Property	ATV	ROSU	SDC	VPM	ADB
λ_{max}, nm	507	507	507	507	507
Beer's law limits (µg mL^{-1})	1.5-10.5	3.2-22.4	1-7	1.4-9.8	3.4-23.8
Molar absorptivity	$1.24x10^4$	$4.8x10^5$	$1.32x10^5$	$0.64X10^5$	$0.35X10^5$
Sandell's sensitivity (µg cm^2)	0.0144	0.0055	0.0056	0.0078	0.0168
Variance $(S_a)^2$	0.000002	0.000006	0.000002	0.00006	0.00004
Limit of detection µg mL^{-1}	0.0530	0.8198	0.0888	0.2003	0.0481
Limit of quantification µg mL^{-1}	0.1608	2.4843	0.2692	0.6070	0.1458
Regression equation, Y**					
Intercept, (a)	0.055	0.055	0.015	0.015	0.071
Slope, (b)	0.069	0.032	0.180	0.128	0.048
Correlation coefficient, (r)	0.9995	0.9994	0.998	0.999	0.998
Standard deviation of intercept (S_a)	0.0011	0.0079	0.0049	0.0078	0.0007
Standard deviation of slope (S_b)	0.0012	0.0011	0.0028	0.0007	0.0162

Limit of determination as the weight in µg per mL of solution, which corresponds to an absorbance of A = 0.001 measured in a cuvette of cross-sectional area 1 cm^2 and path length of 1 cm. Y** = a+bX, where Y is the absorbance and X concentration of drugs in µg per mL.

Accuracy and precision

The accuracy and precision of the methods were established by analyzing the pure drug solution at 6 different levels (with working limits). The relative error (%) which is a measure of accuracy & RSD (%) a measure of precision are summarized in Table II and reveal the high accuracy and precision of the methods.

Table II
Determination of accuracy and precision of the methods on pure drug samples

Drug	Taken (µg/mL)	Found (µg/mL)	error (%)	Recovery (%)	RSD (%)	Proposed method Mean ± SD
ATV	1.5	1.51	0.66	99.33	0.1705	99.51 ± 0.1697
	3.0	3.01	0.33	99.67		
	4.5	4.48	0.44	99.55		
ROSU	3.2	3.19	0.31	99.68	0.2107	99.87 ± 0.2104
	6.4	6.39	0.15	99.84		
	9.6	9.61	0.10	100.10		
SDC	1.0	1.00	0.00	100.00	0.5849	100.06 ± 0.5853
	2.0	1.99	0.50	99.50		
	3.0	3.02	0.67	100.67		
VPM	1.4	1.41	0.71	100.71	0.5357	100.19± 0.5368
	2.8	2.79	0.36	99.64		
	4.2	4.21	0.24	100.24		
ADB	3.4	3.39	0.29	99.70	0.2418	99.98 ± 0.2418
	6.8	6.81	0.15	100.14		
	10.2	10.21	0.09	100.09		

Robustness and ruggedness

To evaluate the robustness of the methods, volume of Sulphuric acid was slightly altered. The reaction time (after adding $KMnO_4$, time varied was 10 ±2min) and the time after addition of dye is slightly changed. To check the ruggedness, analysis was performed by three different analysts and on three different spectrophotometers by the same analyst.

Application to formulations

The proposed methods were applied to the determination of drugs in tablets. The results in Table III showed that the methods are successful for the determination of drugs and that the excipients in the

dosage forms do not interfere. The results are compared to the available validated reported [7,21,37,48 & 57] methods on each drug and the results agree well with the claim and also are in agreement with the results obtained by the literature method. Statistical analysis of the results using Student's t-test for accuracy and F-test for precision revealed no significant difference between the proposed methods and the literature method at the 95 % confidence level with respect to accuracy and precision. Recovery experiment was performed via standard addition technique to ascertain the accuracy and validity of the proposed methods. To a fixed and known amount / concentration of drug in tablet powder, pure drug was added at three levels (50, 100 and 150 % of the level present in the tablet) and the total was found by the proposed methods. Each experiment was repeated six times and the percent recovery of pure drugs added (Table III) was within the permissible limits showing the absence interference by the inactive ingredients in the assay.

Table III
Results of assay of tablets by the proposed methods and statistical evaluation and recovery experiments by standard addition method

Tablets	Drug in tablet µg mL^{-1}	Drug added `µg mL^{-1}	Total found µgmL^{-1}	Error (%)	Recovery (%)	RSD (%)	Referencemethod Mean± SD	Proposed method Mean± SD
Atrovastatin Calcium (ATV)	0.50	1.5	1.99	0.50	99.50	0.4978	100.028 ±0.4979	100.028 ±0.4979
	0.50	3.0	3.49	0.28	99.71			
	0.50	4.5	5.02	0.40	100.40			
	1.5	0.0	1.51	0.66	100.66			
	3.0	0.0	3.01	0.33	100.33			
	4.5	0.0	4.48	0.44	99.55			
Rosuvas (ROSU)	0.50	3.2	3.71	0.27	100.27	0.1822	99.979 ±0.1822	99.979 ±0.1822
	0.50	6.4	6.89	0.14	99.85			
	0.50	9.6	10.08	0.19	99.80			
	3.2	0.0	3.2	0.00	100.00			
	6.4	0.0	6.39	0.15	99.84			
	9.6	0.0	9.61	0.10	100.10			
Sildenafil (SDC)	0.50	1.0	1.49	0.66	99.33	0.6813	100.2 ±0.6828	100.2 ±0.6828
	0.50	2.0	2.51	0.40	100.40			
	0.50	3.0	3.48	0.57	99.42			
	1.0	0.0	1.00	1.00	101.00			
	2.0	0.0	2.01	0.50	100.50			
	3.0	0.0	3.01	0.66	100.66			
Vasopten (VPM)	0.50	1.4	1.89	0.52	99.47	0.3830	99.99 ±0.3830	99.99 ±0.3830
	0.50	2.8	3.31	0.30	100.30			
	0.50	4.2	4.68	0.42	99.57			
	1.4	0.0	1.40	0.00	100.00			
	2.8	0.0	2.81	0.35	100.35			
	4.2	0.0	4.21	0.23	100.23			
NORVASC (ADB)	0.50	3.4	3.89	0.25	99.74	0.2175	101.16±0.047	99.98 ±0.2175
	0.50	6.8	7.31	0.13	100.13			
	0.50	10.2	10.68	0.18	99.81			
	3.4	0.0	3.41	0.29	100.29			
	6.8	0.0	6.79	0.14	99.85			
	10.2	0.0	10.21	0.09	100.09			

Table IV
F-test and t-test values

	Atrovastatin(ATV)	Rosuvas (ROSU)	Sildenafil (SDC)	Vasopten(VPM)	Norvasc(ADB)
F-test*	0.2479 (4.7571)	0.0332 (4.7571)	0.4662 (4.7571)	0.1466 (4.3874)	0.0473 (4.2839)
t-test**	0.7729 (3.182)	1.1596 (3.182)	0.7812 (3.182)	0.9917 (2.571)	1.876 (2.447)

**t- test and **F-test values from literature.*

CONCLUSION

The present study described the successful development of new, simple, sensitive, selective, accurate and rapid spectrophotometric method for the accurate determination of the above drugs in its pharmaceutical form by using $KMnO_4$ as the oxidizing reagent. There is no interference from additives and excipients. The method thus can be used in the determination of these drugs in pure and pharmaceutical formulations. So, it is the best alternative to the reported methods for the determination of these drugs.

ACKNOWLEDGEMENT

Authors are grateful to Head, Department of Chemistry, Osmania University for providing facilities. Authors are also thankful to G. Venkateshwarlu, Dept of Chemistry, Osmania University for helpful discussions. One of the authors Rajitha Balusani is thankful to SERO-UGC, Hyderabad for the financial assistance in the form of Minor Research Project.

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