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VALIDATED KINETIC SPECTROPHOTOMETRIC DETERMINATION OF DRUGS USING ALKALINE POTASSIUM PERMANGANATE OXIDATION

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Keywords:

Bendamustine hydrochloride, Ciprofloxacin hydrochloride, Dorzolamide hydrochloride, Pantoprazole sodium, Warfarin sodium, Kinetic method, Alkaline $KMnO_4$, Spectrophotometry, Determination

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ABSTRACT: A simple and sensitive kinetic method is described for the determination of drugs *viz.*, Bendamustine hydrochloride (BEN), Ciprofloxacin hydrochloride (CIP), Dorzolamide hydrochloride (DOR), Pantoprazole sodium (PAN), Warfarin sodium (WAR). This method is based upon a kinetic investigation of drug oxidation with alkaline potassium permanganate. Kinetics of the oxidation reaction is followed spectrophotometrically, as one of the reaction product, Mn (VI), absorbed at 610 nm. All variables affecting color development have been investigated and the conditions optimized. Among the methods applied were the Initial rate and fixed-time methods. Accounting for the applicability, the sensitivity, values of correlation coefficient (r) and intercept (a), the Fixed-time method is selected for these five drugs assay. The absorbance-concentration plots were rectilinear within the range of 8.5-51 µg.mL^{-1} for BEN 1-6 µg.mL^{-1} for CIP, 10-60 µg.mL^{-1} for DOR 20-120 µg.mL^{-1} an7-42 µg.mL^{-1} for WAR. The statistical data for the results challenged for the robustness of the fixed-time method.

INTRODUCTION:

Bendamustine Hydrochloride: Bendamustine hydrochloride (BEN) **Fig. 1A** chemically known as 4-{5-[bis-(2-chloroethyl) amino]- 1-methyl-1Hbenzimidazol-2-yl} butanoic acid, is an active nitrogen mustard [1]. It was used for the treatment of patients with chronic lymphocytic leukemia [2]. It contains mechlorethamine group and benzimidazole heterocyclic ring with a butyric acid substituent. Mechlorethamine and its derivatives form electrophilic alkyl groups. These groups form covalent bonds with electron-rich nucleophilic moieties, resulting in interstrand DNA cross-links. The bifunctional covalent linkage can lead to cell death *via* several pathways [3]. It was active against both quiescent and dividing cells [4-7]. It was approved by the US food and drug administration (FDA) for chronic lymphocytic leukemia in March 2008 [8]. The methods reported for quantitative determination of Bendamustine in bulk or pharmaceutical formulations include HPLC [9], LCMS [10], Ion association complex method [11], LC method [12].

Ciprofloxacin Hydrochloride: Ciprofloxacin (1 - cyclopropyl - 6 - fluoro-1,4 - dihydro - 4 - oxo - 7-(1-piperazinyl) - 3-quinolone carboxylic acid) **Fig. 1B** is a synthetic fluoroquinolone antimicrobial agent. It is a relatively new, a second-generation fluoroquinolone antibiotic with an expanded spectrum of activity against Gram-positive and Gram-negative bacteria. This antimicrobial act through the inhibition of DNA-gyrase, an enzyme that is critical to bacterial chromosome replication.

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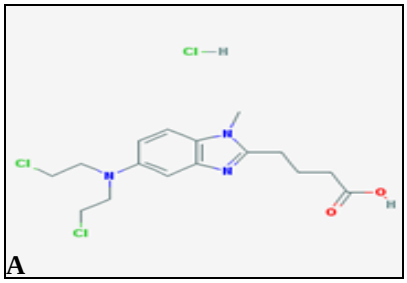
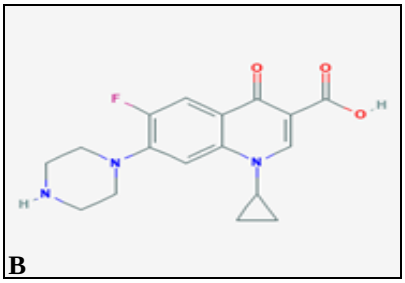
Ciprofloxacin, like other fluoroquinolones, contains a piperazine group at position 7 of the 4-quinolone nucleus, which results in activity against Pseudomonas aeruginosa. It is used in a wide range of infections of the urinary, respiratory and gastrointestinal tracts, as well as in skin structure and ocular infections [13]. The reported methods for ciprofloxacin includes UV detection [14], fluorescence detection [15], HPTLC [16], fluorimetry [17], capillary electrophoresis [18], immune assay [19], chemo-luminescent [20] detection, Solid-phase spectrophotometry (SPS) has been found to be useful for the determination of both inorganic and organic species [21] by complex colored formation. The determination of species by direct measurement of its intrinsic ultraviolet absorption [22].

Dorzolamide Hydrochloride: Dorzolamide HCl is a carbonic anhydrase inhibitor used to lower increased intraocular pressure in open-angle glaucoma and ocular hypertension. Dorzolamide HCl is chemically [(4*S*, 6S)-4-(Ethyl amino)-6-methyl-5, 6-dihydro-4*H*thieno[2,3*b*] thiopyran-2- sulphonamide 7, 7-dioxide hydrochloride]. It is an anti-glaucoma agent and topically applied in the form of eye drops. A literature survey revealed that very few methods were developed; they are UV spectroscopic method [23], HPLC [24, 25], RP-HPLC [26].


A

Bendamustine hydrochloride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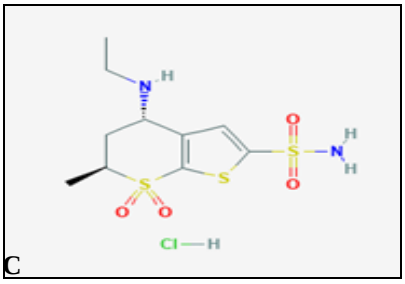
Ciprofloxacin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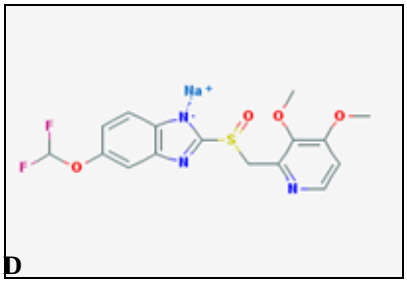
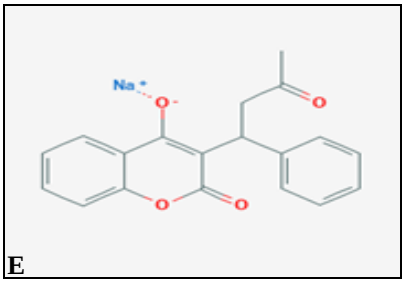
Dorzolamide hydrochloride


D

Pantoprazole sodium


E

Warfarin sodium

FIG. 1: STRUCTURE OF THE DRUGS

Pantoprazole Sodium: Pantaprazole **Fig. 1D** is 5-(Difluoromethoxy) - [[(3,4- dimethoxy-2-Pyridiynyl) Methyl] sulphinyl] -1H - benzimidazole. It is a gastric proton pump inhibitor. The gastric proton pump inhibitors have a structural resemblance to H_2 antagonists. They are the prodrugs and after absorption get converted to reactive thiophilic sulphonamide cations. The sulphonamide reacts with the H^+ /K^+ AT P-ase, forming a covalent, disulfide linkage, thus irreversibly inactivating the enzyme [27]. The methods reported for quantitative determination of Pantoprazole in bulk or pharmaceutical formulations include titrimetry, colorimeter [28-31], and high-performance liquid chromatography [32-35]. This paper presents the simple, accurate and reproducible UV spectro-photometric methods for determination of Pantoprazole in the tablet dosage form. In the literature survey, it is found that methods have been reported for estimation of Pantoprazole and domperidone in combined tablet dosage form by UV spectro-photometry [36]. But to the best of our knowledge, there is no work in the literature reported about the UV spectrophotometric method for the analysis of Pantoprazole in pharmaceutical formulations using water as a solvent.

Hence, the authors have attempted to develop a simple and rapid UV spectrophotometric method for the estimation of Pantoprazole in the bulk drugs and pharmaceutical formulations taking water as a solvent.

Warfarin Sodium: Active Pharmaceutical Ingredient (API) Warfarin Sodium can be found in three formulations: as a tablet, oral suspension (syrup) with the strength of 1 mg/mL and dilution for injections. Warfarin Sodium **Fig. 1E** is the sodium salt of 3-(α- acetonylbenzyl)-4-hydroxycoumarin. The pharmacologic function of the compound is an anticoagulant that inhibits the synthesis of Warfarin K-dependent coagulation factors. The treatment aims at preventing further extension of the formed clots and secondary thromboembolic complications that may result in serious and possibly fatal sequelae [37]. Two solid forms of Warfarin sodium, amorphous and crystalline clathrate [38], are known to exist. The crystalline clathrate form is a Warfarin Sodium-isopropyl alcohol complex. It is has also been reported that Warfarin Sodium is a true 2-propanol solvate, not a clathrate, which it is transformed to the amorphous state through an intermediate crystalline step. Both forms are used as APIs in pharmaceutical formulations and the most common method for quantitative analysis also adopted by Pharmacopoeia [39], is High-Pressure Liquid Chromatography (HPLC), which is not capable of identifying if the measured quantity refers to crystalline or to amorphous Warfarin sodium. A comparison of various techniques used for estimation of above drugs regarding sensitivity and reproducibility are presented in **Table 1**.

TABLE 1: COMPARISON OF VARIOUS TECHNIQUES

Name of the drug	Method	Sensitivity	Recovery
BEN	1. Spectrophotometry	5-40 µg mL^{-1}	99.81%
	2. LC	0.03-0.6µg mL^{-1}	98.3%
	3. RP-HPLC	1-10 µg mL^{-1}	98.9%
	4. Ion association complex formation method	2.5-120.5 µg mL^{-1}	99.9%
CIP	1. HPLC	90-150 µg mL^{-1}	98.2%
	2. UPLC	6.33-50.69 µg mL^{-1}	98.39%
	3. Spectrophotometry	16-96 µg mL^{-1}	99.58%
	4. FTIR Spectrophotometry	5-150 µg mL^{-1}	98.65%
DOR	1. UV Spectrophotometry	10-50 µg mL^{-1}	99.31%
	2. RP-HPLC	20-100 µg mL^{-1}	98.77%
PAN	1. UV Spectrophotometry	5-70 µg mL^{-1}	99.07%
	2. RP-HPLC	1-100µg mL^{-1}	96.6%
	3. LCMS	4.5-2800 ng mL^{-1}	99.1%
	4. Bioanalytical method	10-3000 ng mL^{-1}	99.27%
	5. Colorimetric method	10-50 µg mL^{-1}	100.01%
WAR	1. HPLC	2.5-10 ng mL^{-1}	91.8%
	2. UPLC MS	1-10 ng mL^{-1}	89.6%
	3. GLC	2-3µL	97.26%
	4. Raman spectroscopic method	1mg mL^{-1}	

EXPERIMENTAL:

Instrumentation: The UV-VIS spectra of the study have been recorded on ELICO SL 210 double beam Spectrophotometer using quartz cells of 10 mm path length.

A Dhona 200 single pan electrical balance is used for weighing the samples.

Materials: Analytical grade $KMnO_4$, NaOH and triple distilled water was used for preparing solutions for the study.

Preparation of Drug Solution: A stock solution of each drug-containing 2000 µg mL^{-1} was initially prepared and further diluted to get working concentrations.

$KMnO_4$ Solution: A stock solution of $KMnO_4$ is prepared by dissolving 0.158 gm of a pure sample of $KMnO_4$ in 100 mL triple distilled water.

Standardization of $KMnO_4$: The standardization of $KMnO_4$ solution is carried out by titration against a standard solution of sodium oxalate. The reaction is

$$2MnO_4^- (aq) + 8H^+ (aq) + 5\ e^- \rightarrow 2Mn^{2+} + 4H_2O\ (l)$$

$$2\ KMnO_4 + 5Na_2C_2O_4 + 8H_2SO_4 \rightarrow K_2SO_4 + 2MnSO_4 + 5Na_2SO_4 + 10CO_2 + 8H_2O$$

NaOH Solution: 0.5M NaOH solution is prepared by dissolving 20 gm of NaOH in 1000 mL triple

distilled water. The same is standardized by titrating against standardized HCl solution.

Method Development: The method depends on the oxidation of the drug with alkaline potassium permanganate (1×10^{-2} M) to produce Manganate ion which absorbs at 610 nm and formed a basis for quantification of the drug. A solution of 0.45 - 0.5 M NaOH is used to produce required alkalinity to the solution. Linearity and calibration curves are determined from initial rate and fixed time methods.

Procedure for Kinetic Study: A stock solution of each drug-containing 2000 µg mL^{-1} was prepared as mentioned earlier. The drug solutions were further diluted to get the required concentrations for the kinetic study. 8 mL of this drug solution was transferred into 10 mL calibrated flask, 1ml of $KMnO_4$ (1×10^{-2}M) and 1mL of NaOH was added. After shaking for 10 sec the solution was transferred to a cuvette and was placed in the sample compartment. Similarly, prepared blank solution was placed in the reference compartment. The absorbance of this sample was measured at 2, 5, 10, 15, 20, 25 and 30 min. The procedure is repeated with 7 mL, 6mL, 5 mL, 4 mL, 3 mL, 2 mL and 1 mL of drug solutions by making up the remaining volume with distilled water. Absorbance-time curves **Fig. 2** were constructed.

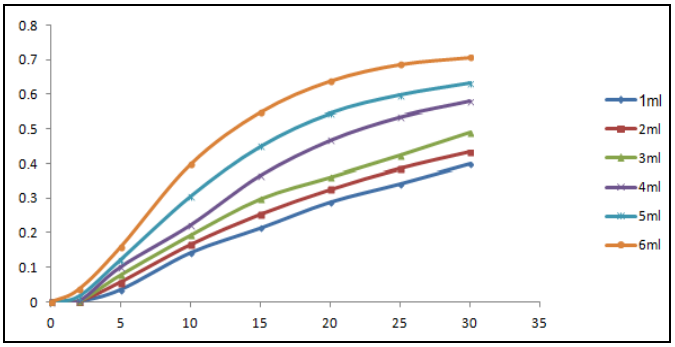


FIG. 2: ABSORBANCE-TIME CURVES FOR THE REACTION OF DRUGS WITH ALKALINE $KMnO_4$

Recommended Procedures:

Initial Rate Method: Aliquots of 8.5-51 µgmL^{-1} BEN, 1-6 µgmL^{-1} CIP, 10-60 µgmL^{-1} DOR, 20-120 µgmL^{-1} PAN and 4-42 µgmL^{-1} WAR solutions were transferred into a series of 10 ml calibrated volumetric flasks. To each flask was added 1.0 mL of 0.5 M NaOH followed by 1.0 mL of 0.01 M $KMnO_4$ and the volume was made up to the mark with double distilled water at room temperature. After mixing, the contents of each flask were immediately transferred to the spectrophotometric cell and the increase in absorbance of the colored manganate ion as a function of time was measured at 610 nm. The initial rate of the reaction (n) at different concentrations was evaluated by measuring the slope of the tangent to the absorbance-time curve.

Fixed Time Method: In this method, the absorbance of a green colored solution containing varying amounts of drugs as mentioned above for initial rate method were measured at a preselected fixed time, 15 min.

Procedure for Assay of Pure Drug: To test the accuracy and precision of the methods developed, pure sample solutions containing the drug in the Beer's Law limit were chosen, and kinetics of the reaction were studied. For this study 9, 13, 26 and 39 µgmL^{-1} of BEN; 1.5, 2.5, 3.5 and 4.5 µgmL^{-1} of CIP; 12, 24, 36 and 40 µgmL^{-1} of DOR; 25, 35, 45 and 55 µg mL^{-1} of PAN; 9, 15, 27 and 45 µgmL^{-1} of WAR were chosen for kinetic study other experimental details being common. Initial rate and a fixed time of 15 min were chosen to estimate the amount found.

Procedure for Analysis of Pharmaceuticals:

Bendamustine Hydrochloride: Bendit (lyophilized powder – marketed formulations of Natco Pharma Limited, Hyderabad), an amount equivalent to 50 mg of Bendamustine hydrochloride was dissolved into 10mL of methanol and filtered through a Whatman filter paper (no. 42). The filtrate was transferred into 100 mL volumetric flasks and made up to the mark with distilled water. Kinetics runs were performed using 12, 18, 25 and 40 µgmL^{-1} of Bendamustine, other experimental details being common. Initial rate and a fixed time of 15 min were chosen to estimate the amount found.

Ciprofloxacin Hydrochloride: An accurately weighed two capsules (Cifran-od-1gm) were taken, and the granules in the capsules were finely powdered, weighed, a portion equivalent to 250 mg was transferred quantitatively into 100 mL volumetric flask, sonicated for 15 min, completed to volume with distilled water. A stock solution containing 2.5 mgmL^{-1} was further diluted to get the required concentration (2.4 µgmL^{-1}) for

pharmaceutical analysis. Kinetics runs were performed using 2.4, 3.6, 4 .8 and 5.2 µgmL^{-1} of ciprofloxacin other experimental details being common. Initial rate and a fixed time of 15 min were chosen to estimate the amount found.

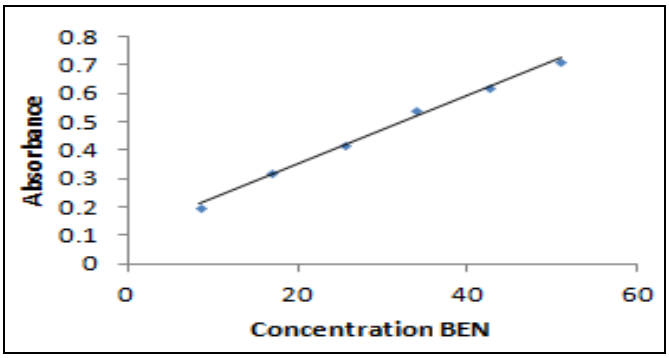
Dorzolamide Hydrochloride: The commercially available eye drops contains 2% Solution of Sterile Dorzolamide HCl (20 mg/mL). From this eye drop 1mL Solution was carefully transferred into volumetric flask of 20 mL capacity containing 10 mL of the diluent and sonicated for 5 min, and the the final solution was made with the same diluent to get the solution of 1000 µg mL^{-1}. From this solution, 10 mL was taken in 100 mL standard volumetric flask and diluted to 100 ml with diluent to give a solution of 100 µg mL^{-1}. From this stock solution, various dilutions (10, 16, 22 and 28µg mL^{-1}) of solution were prepared and analyzed.

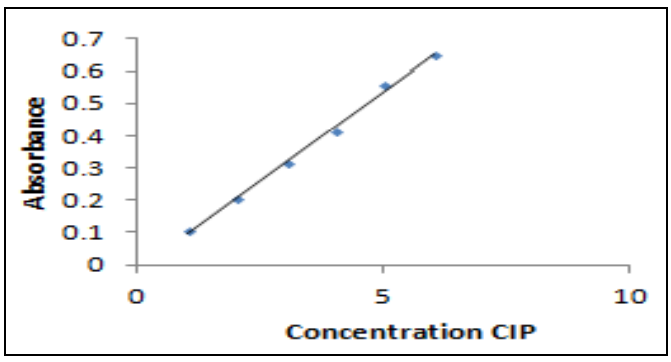
Pantoprazole Sodium: For analysis of commercial formulations, five tablets (Protocent-40 mg) were taken and powdered. Tablet powder equivalent to 400 mg of Formulation was transferred into 100 ml volumetric flask and dissolved in 0.5 M NaOH. Then the solution was sonicated for 30 min and filtered. 1.25 ml from the filtrate were taken and further diluted with 0.5 M NaOH to form 12 µg mL^{-1}. Kinetics runs were performed using 12, 18, 25 and 40 µgmL^{-1} of Pantoprazole, other experimental details being common. Initial rate and a fixed time of 15 min were chosen to estimate the amount found.

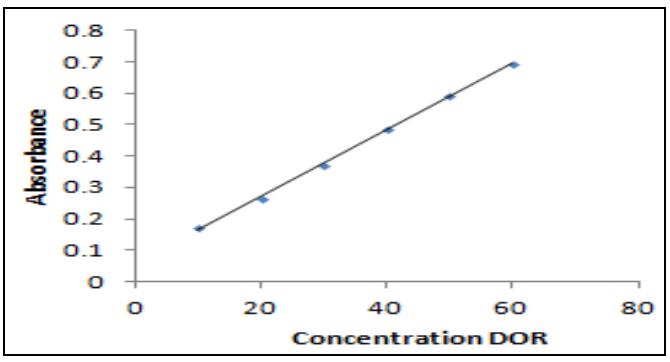
Warfarin Sodium: To see the feasibility of the proposed method for estimation of Warfarin in marketed pharmaceutical formulations, thirty tablets (Sofarin- 5mg) were weighed, the average weight determined and crushed into fine powder. A quantity of tablet powder equivalent to 20 mg of Warfarin was transferred into 100 mL volumetric flask containing 50 mL water, shaken manually for 10 min; volume was adjusted to mark with the same solvent and filtered through Whatman filter paper no. 1. The appropriate aliquots were transferred to 10 ml volumetric flask; volume was adjusted to the mark with the same solvent to obtain a concentration of 13 µgmL^{-1}. Kinetics runs were performed using 13, 27, 39 and 942 µgmL^{-1} of Warfarin, other experimental details being common. Initial rate and a fixed time of 15 min were chosen to estimate the amount found.

RESULTS AND DISCUSSION:

Construction of Calibration: The absorbance data of kinetic runs at 2 min and 15 min are used to construct calibration. The average relative responses of 5 replicates were evaluated. The absorbance is falling within 95% to 105% of average relative responses only are considered in the construction of the calibration curve **Fig. 3**.







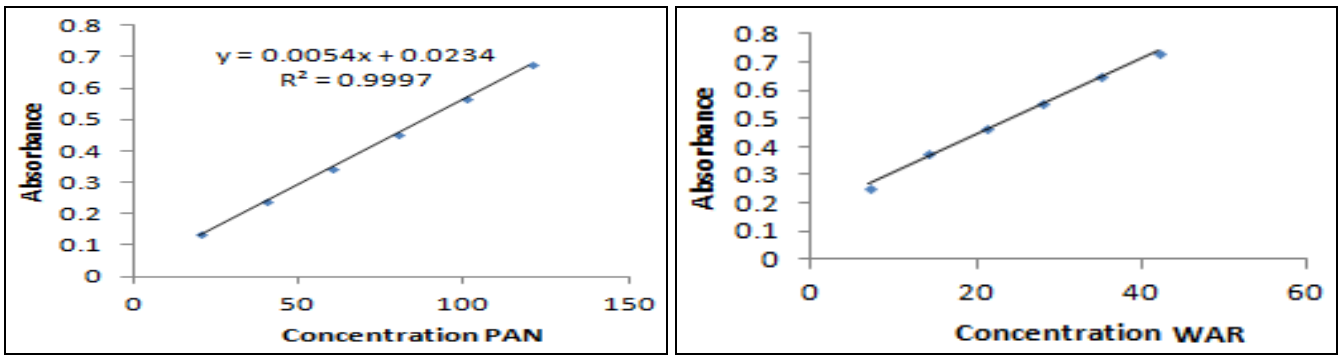


FIG. 3: CALIBRATION CURVES OF THE DRUGS

The limits of Beer's law, slope, intercept, correlation coefficient, Sandell's sensitivity and regression equation for each drug are tabulated in **Table 2**.

TABLE 2: ANALYTICAL PARAMETERS FOR DETERMINATION OF DRUGS BY OXIDATION WITH ALKALINE $KMnO_4$

Name of the drug property	BEN	CIP	DOR	PAN	WAR
λ_{max}	610	610	610	610	610
Beer's law limits(µg ml^{-1})	8.5-51	1-6	10-60	20-120	7-42
Sandell's sensitivity (µg cm^{-2})	0.000083	0.1	0.001	0.2	0.076
Std.dev. of intercept	0.002517	0.002517	0.004163	0.000577	0.003215
LOD (µg mL^{-1})	0.692	0.553	0.236	0.380	0.816
LOQ (µg mL^{-1})	0.224	1.678	0.717	1.154	2.47
Slope, b	0.012	0.110	0.01	0.005	0.013
Intercept, a	0.112	-0.015	0.058	0.023	0.175
Correlation co-efficient	0.996	0.997	0.999	0.999	0.996
Regression equation $Y=c+bx^*$					

X = Concentration of the Drug, (µg mL^{-1})

TABLE 3: RECOVERY STUDIES TO EVALUATE ACCURACY AND PRECISION FOR THE DETERMINATION OF DRUGS BY REDOX REACTION WITH ALKALINE $KMnO_4$

Name of the drug	Amount took µg mL^{-1}	Amount found µg mL^{-1}	% recovery	RSD %	Proposed method Mean ± SD	Ref method Mean ± SD	t-test	F-test
BEN	9	9.01	100.1%					
	13	13.02	100.15%	0.0987	100.012 ± 0.098	99.90 ± 0.356	0.665	0.075
	26	25.98	99.92%					
	39	38.99	99.97%					
CIP	1.5	1.49	99.33%					
	2.5	2.49	99.6%	0.4677	99.85 ± 0.467	98.39 ± 1.22	2.504	0.146
	3.5	3.51	100.28%					
	4.5	4.51	100.22%					
DOR	12	12.01	100.83%					
	24	23.98	99.91%	0.4322	100.18 ± 0.434	99.31 ± 0.388	3.344	1.25
	36	36.01	100.02%					
	40	39.99	99.97%					
PAN	25	24.99	99.96%					
	35	35.01	100.02%	0.476	99.99 ± 0.047	98.8 ± 0.91	2.92	0.0027
	45	45.02	100.04%					
	55	54.97	99.94%					
	9	8.99	99.88%					
WAR	15	15.02	100.13%	0.1766	99.90 ± 0.176	97.26 ± 1.89	3.22	0.0086
	27	26.98	99.92%					
	45	44.99	99.97%					

Method Validation: Each method developed for quantification of drugs has been validated regarding precision, accuracy, limit of detection. Limit of quantification, linearity, selectivity, and ruggedness. Absorbance-time curves were drawn, the initial rate and fixed time methods were used to

assess the recovery of the drug. To assess the precision, each experiment was repeated at least 5 times, and accuracy is estimated regarding percent recovery and percent RSD. Excellent percent recovery and RSD being less than 2 for each drug demonstrates accuracy and precision of the methods. Further, t-test and F-test values have also been calculated using a standard reference method. The t-test and F-test values are less than that their permissible range is indicating high accuracy and precision of the methods **Table 3**. 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.

$$LOD = 3.3\ s/S$$

Wheres = standard deviation of intercept (n=5)
S = slope of linearity plot

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

$$LOQ = 10s/S$$

Limits of Linearity of calibration curves are mentioned in **Table 1** 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 the resistance of method for a small change in variables like instrument and analyst or both. To test the ruggedness of the method absorbance data were collected using 3 different instruments and 2 analysts. No significant changes were observed either by change of instrument or analyst; hence the method may be treated as rugged.

Factors Affecting Absorbance:

Effect of Concentration of $KMnO_4$: The effect of concentration of $KMnO_4$ on the absorbance at a preselected time, 15 min was studied in the range 0.2×10^{-2}M to 1.2×10^{-2}M by keeping the concentration of drug constant. The absorbance increased with increasing the concentration of $KMnO_4$ and became constant at 0.7×10^{-2}M to 0.8×10^{-2}M. Thus, the adoption of 1×10^{-2}M $KMnO_4$ in the final solution proved to be adequate for the maximum concentration of drugs used in the determination process.

Effect of NaOH: The influence of the NaOH concentration examined by taking the fixed concentration of the drug, 1.0 ml of 0.01M $KMnO_4$ solution and varying volumes (0.2 - 1.2 ml) of 0.5 M NaOH. The maximum absorbance was obtained with 0.8 ml of 0.5M NaOH, after which further increase in the volume of NaOH caused no change in absorbance. Hence, 0.8 to 1.0 ml of 0.5M NaOH was used as an optimum value.

Effect of Prolonged Time: The effect of time on the reaction between $KMnO_4$ and the drugs was studied. The absorbance of the reaction mixture was increased with time. The solutions turned turbid after 30-35 min.

Effect of Temperature: At room temperature, the reaction rate of four drugs increased substantially as the color development increased. The higher temperature causes precipitation of MnO_2; therefore, room temperature was selected as the optimum.

Analysis of Pharmaceuticals: To test the applicability of the method developed, a solution of pharmaceutical tablets drug in the Beer's Law limit were chosen, and kinetics of the reaction were studied. For this study 12, 18, 25 and 40 μg ml^{-1} of BEN; 2.4 3.6, 4.8 and 5.2 μg ml^{-1} of CIP; 10, 16, 22 and 28 μg ml^{-1} of DOR; 12, 18,24, and 30 μg ml^{-1} of PAN, 13, 27, 39 and 42 μg ml^{-1} of WAR were chosen for kinetic study other experimental details being common. Initial rate and a fixed time of 15 min were chosen to estimate the amount found. Absorbance-time curves were drawn, initial rate and fixed time methods were used to assess the recovery of the drug in pharmaceuticals. To assess the precision, each tablet analysis was repeated at least 5 times, and accuracy is estimated regarding percent recovery and percent RSD. Excellent percent recovery and RSD being less than 2 for each drug demonstrates the applicability of the methods for pharmaceutical analysis. Further t-test and F-test values have also been calculated using a standard reference method. The closeness of t-test and F-test values are less than that they permissible range was indicating excellent applicability of the methods for pharmaceutical analysis **Table 4**. The excellent recovery studies indicate that methods developed can be applied to pharmaceutical analysis without hesitation.

As defined earlier Sandell's sensitivity of the analyte capable of producing a change 0.001 absorbance unit is a measure of the sensitivity of the method. Lower the Sandell's sensitivity higher is the sensitivity of the method developed.

The Sandell's sensitivity values of drugs presented in **Table 2** indicate that BEN has lowest Sandell's sensitivity and hence is highest sensitivity of the method, they are in the order BEN<DOR <WAR<CIP<PAN.

TABLE 4: APPLICATION OF PROPOSED METHOD FOR THE ANALYSIS OF STUDIED DRUGS IN PHARMACEUTICAL FORMULATIONS BY REDOX REACTION WITH ALKALINE $KMnO_4$

Name of the drug	Amount taken µg mL^{-1}	Amount found µg mL^{-1}	% recovery	RSD %	Proposed method Mean ± SD	Ref method Mean ± SD	t-test	F-test
BEN	12	12.01	100.83%					
(Bendit)	18	18.02	100.11%	0.419	100.21 ± 0.420	99.81 ± 0.53	1.31	0.62
	25	24.99	99.94%					
	40	39.99	99.96%					
CIP	2.4	2.38	99.16%					
(Cifran-od	3.6	3..61	99.5%	0.369	99.61 ± 0.368	99.58 ± 1.25	0.024	0.086
1g)	4.8	4.79	99.79%					
	5.2	52.01	100.01%					
DOR	10	10.01	100.1%					
(Dortas)	16	15.99	99.93%	0.0776	99.98 ± 0.077	98.8 ± 0.88	2.99	0.0079
	22	21.99	99.95%					
	28	27.99	99.96%					
PAN	12	11.99	99.91%					
(Protocent-	18	17.98	99.88%	0.0699	99.94 ± 0.069	99.01 ± 0.445	2.089	0.024
40mg)	24	24.01	100.04%					
	30	29.99	99.96%					
WAR	13	12.98	99.84%					
(Sofarin-	27	27.01	100.03%	0.128	99.95 ± 0.128	98.8 ± 0.68	3.71	0.354
40mg)	39	39.02	100.05%					
	42	41.99	99.97%					

CONCLUSION: $KMnO_4$, an oxidizing agent in the alkaline medium is found to oxidize drugs like BEN, CIP, DOR, PAN and WAR which are soluble in basic medium. One of the oxidizing products namely manganate ion absorbs maximally at 610 nm, whose absorbance is the function of the concentration of the drug. Kinetics of the reaction is followed for quantification, construction of calibration, validation, and optimization of the method.

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