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CONDUCTOMETRIC DETERMINATION OF CATIONIC DRUGS AND PHARMACEUTICALS USING AMMONIUM MOLYBDATE AS PRECIPITATING AGENT

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ABSTRACT: Simple, sensitive, accurate, cost effective and precise Conductometric method for quantitative determination of Five Cationic commercial drugs viz. Ondansetron HCl(OND), Propranolol HCl(PRP), Sertraline HCl(SET), Tramadol HCl (TRA), Levo Cetirizine Di HCl(LEV) were developed. The method was based on the formation of insoluble salt ($[Drug]_6Mo_4O_7$) between the Drug Cation of Drug molecules and Molybdate Anion of Ammonium Molybdate(AMB) solutions. Aliquots of standard drug solution (2.5-15 mL) which is containing 2.5-15 mg pure drug and 2.5x 10^{-3} M Ammonium Molybdate taken in burette was used for titration. The observed conductance reading was taken and corrected conductance i.e. Ω^{-1}correct = Ω^{-1}obs [V1+V2/V1]. A graph of corrected conductivity Vs volume of added titrant was constructed and the endpoint was determined graphically at the intersection of two lines. The amount of drugs under study was calculated according to the equation for amount of drug = V.M.R / N. The proposed method was successfully applied in the determination of the above five metal anionic Drugs and Pharmaceutical formulations, with results in close agreement at a 95% confidence level with those obtained using spectrophotometric determination method.

KEYWORDS: Anionic Drugs, Conductometric, Determination, Ammonium Molybdate, Hydrochloride.

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1.INTRODUCTION

Ondansetron (Fig.1a), is chemically 9-methyl-3-[(2-methyl-1-yle 1H-imidazol] -2-methyle) methyl) - 2, 3-dihydro 1H-carbazol 1-4-one -2, 3-dihydro; hydrochloride. OND mainly is used in the

treatment of cancer chemotherapy and radiation therapy. OND stimulates its response in stomach flu and also effect on motion sickness. A number of methods like Reverse Phase-HPLC [1-2], HPLC [3-4], UV-Spectrophotometry [5-6], Capillary Zone Electrophoresis [7], Liquid Chromatography[8] are available for the estimation of OND in pharmaceutical dosage forms. Propranolol(Fig.1b) is chemically, 1-[(1-isopropylamino]-3-(naphthalen-1-2-methoxyethyl) propan-2-ol. PRP is used in the treatment of cardiac dysrhythmias and angina pectoris. PRP may work by stabilizing windpipe, arteriey. A few analytical methods were determined for PRP such as RP-HPLC [9], HPLC [10-14], HPTLC[15]and UV- Spectrophotometry [16-21], Spectrofluorimetry [22], Atomic absorption spectroscopy[23-24] and voltametry [25], NMR[26] methods have been reported for estimation of PRP in the literature survey. Sertraline hydrochloride (Fig.1c) is also called as serotonin reuptake inhibitor. SET is used to treatment of depression, obsessive-compulsive disorders and depression relapses. Sertraline HCl regulates brain noradrenaline and indoleamine receptors in animals. Some methods have been reported for the determination of SET in pharmaceuticals dosage forms by RP-HPLC [28-31], HPLC [32-35], RP-LC [36]and UV- Spectrophotometry [37-40] and GC-HS[41]. Tramadol hydrochloride (Fig.1d), chemically cis-2-dimethyl amino methyl-1-(3methoxy phenyl) cyclo hexanol hydrochloride. It is a non- selective and non-steroidal anti-inflammatory drug. TRA used in the treatment of arthritis, restless legs syndrome. According to Literature review, some analytical techniques have shown that there are various techniques described for analysis and determination of Tramadol hydrochloride such as UV-Spectrophotometry [42-48], Extractive Spectrophotometry [49], RP-HPLC[50-52], HPTLC[53-54] conductometry [55], Zone elcetrophoresis [56], Gas Chromatography-MS[57], Thin Layer Chromatography [58], Potentiometry[59], colorometry[60]. Levo Cetirizine di HCl (Fig.1e) chemically is [2-[4-[(4-chlorophenyl) phenyl methyl]-1 piperazinyl] ethoxy] acetic acid di HCl. Cetirizine di HCl is belong to the group of second generation h1 antagonist, inhibits allergic reaction mediated by histamine. It used to relief of itching of eyes, sneezing, itching of the nose or throat problems due to respiratory allergies. Some analytical techniques had been constructed for dugs quantification such as Reverse Phase-High performance Chromatography(RP-HPLC)[61-63], HPLC[64-65], UV Spectrophoto metry[66], Ion exchange resigns method[67], chemiluminiscence[68] for Cetirizine di HCl. Through survey of literature on the above mentioned anionic drugs revealed that Conductometric determination based on the use of Ammonium Molybdate as Precipitating agent [69-72] have not been yet reported. The present work is an attempt to develop accurate, simple, sensitive, and cost effective method for the quantitative analysis of the above drugs.

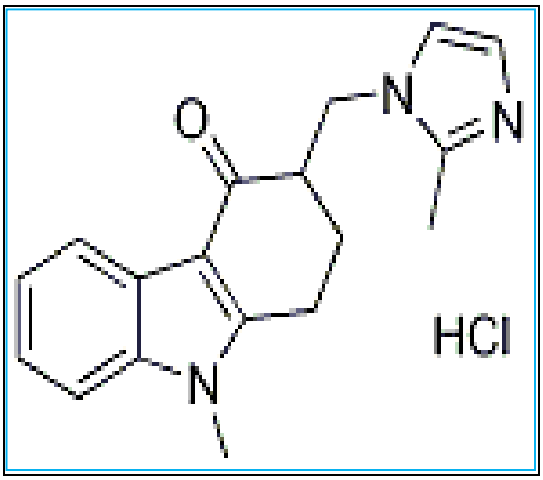

Fig.1a. Structure of OND

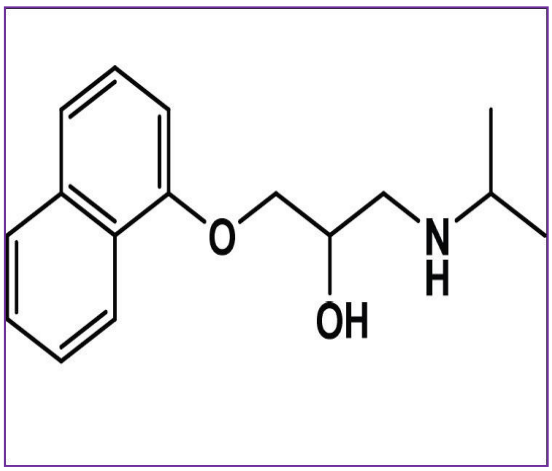

Fig.1b. Structure of PRP

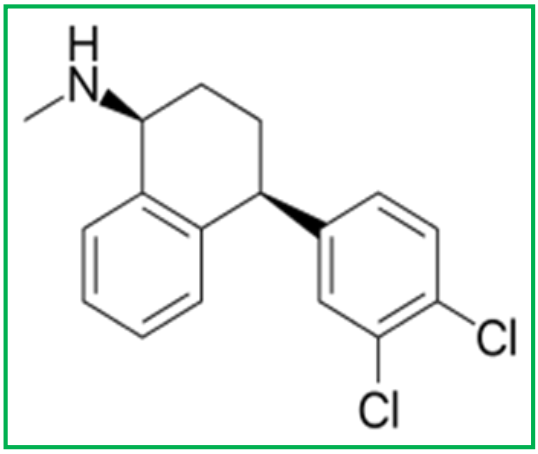

Fig.1c. Structure of SET

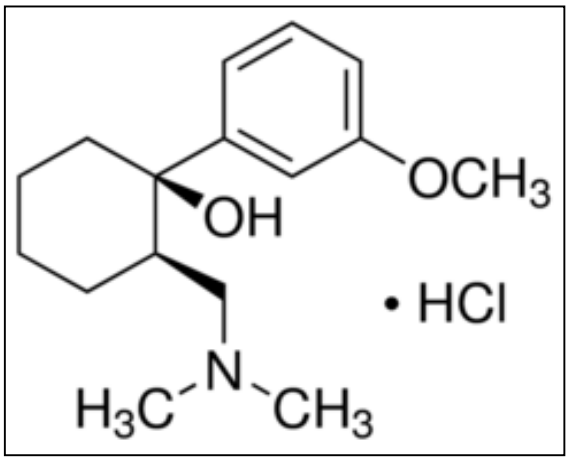

Fig.1d. Structure of TRA

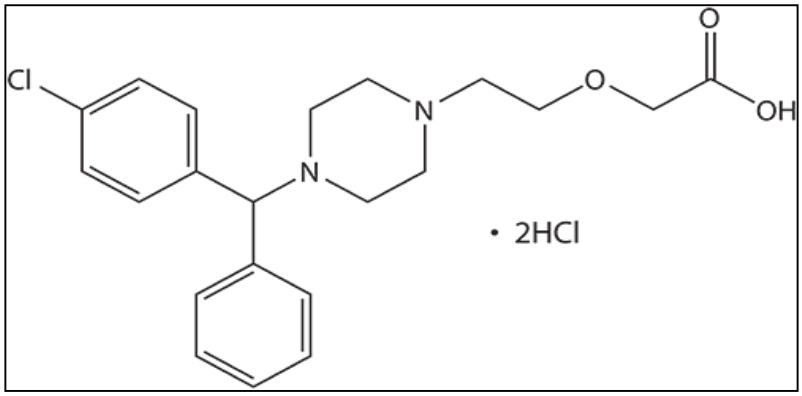

Fig.1e. Structure of LEV

Fig.1. Drug Structures

2. MATERIALS AND METHODS

2.1. Instruments

Conductance for the study required has been measured by using Systronics Conductometer 306 portable conductivity /TDS meter. AC-C10 dipped type Conductometer Cell was used with a cell constant Kcell of 0.97 in the study. A Dhona 200 electrical balance which is having single pan is used for weighing all the samples.

2.2. Materials and Reagents

All reagents used were of analytical-reagent grade and distilled water was used throughout the investigation.0.309gm of Ammonium Molybdate is dissolved in 100ml double distilled water to get 2.5x 10-3 M of Ammonium Molybdate.7.54 gm. of KCl was dissolved in 1000ml double distilled water to get 0.1M KCl. Standard drug solution (200 μg mL^{-1}) was prepared by dissolving 20 mg of drug with distilled water to the mark in 100 ml standard flask. The stock solution was diluted appropriately to get the working concentration.

2.3. Method development

Aliquots of standard drug solution (2.5-15 mL) containing 2.5-15 mg pure drug were transferred to 50 ml calibrated flasks volumes were made up to the mark using double distilled water. The contents of the flask were transferred to a beaker. The conductivity cell was immersed in it and 0.0025 M Ammonium Molybdate taken in burette was used for titration. The conductance reading was taken subsequent to each addition of titrant after stirring for 2 min and corrected for dilution effects by means of the following equation, assuming that conductivity is a linear function of dilution.

$$\Omega_{-1\ correct} = \Omega_{-1obs}\,[V_1+V_2/V_1]$$

Where Ω-1correct is the corrected electrolytic conductivity, Ω-1obs is the observed electrolytic conductivity, V1 is the initial volume and V2 is the volume of reagent added. A graph of corrected conductivity vs. volume of added titrant was constructed and the endpoint was determined graphically at the intersection of two lines (Fig.2 to Fig.6).

The amount of drugs under study was calculated according to the following equation

$$\text{Amount of drug} = V.M.R / N$$

Where, V is volume (mL) of titrant, M is molecular weight of drug, R is molar concentration of titrant and N is number of moles of titrant consumed by one mole of drug. Based on the drug taken vs Drug found, calibration curve were constructed for the five Drugs (Fig.7).

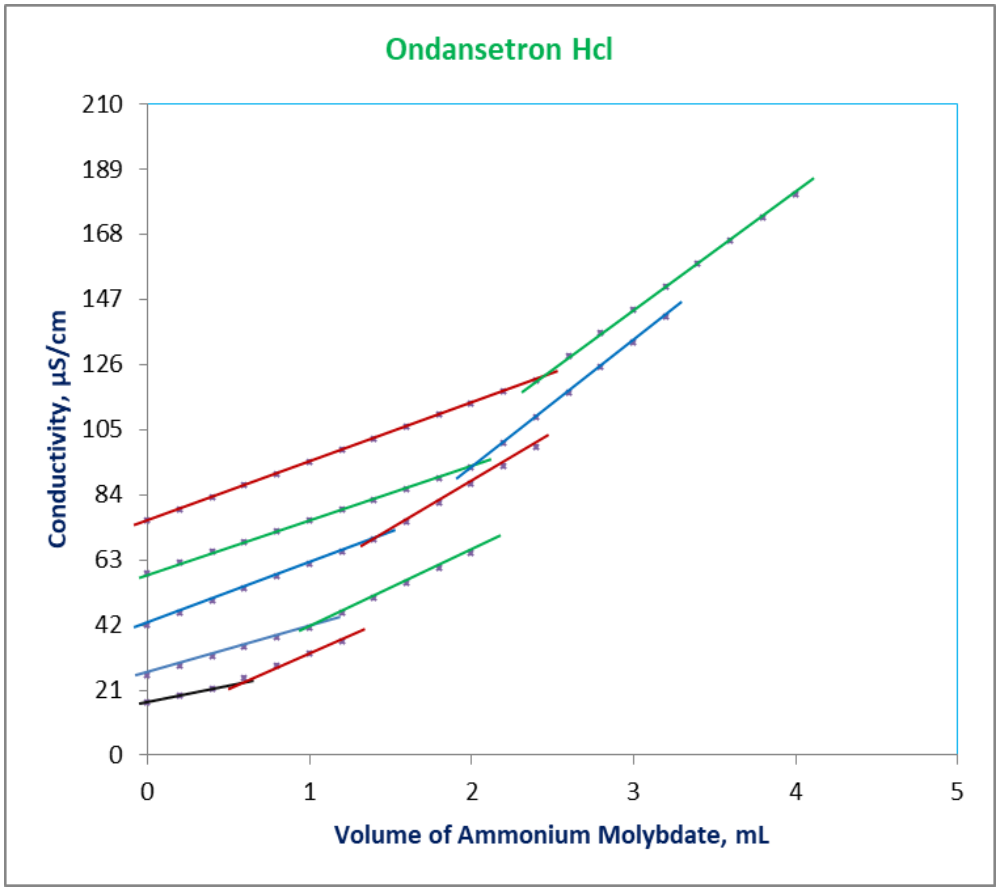

Fig.2.Conductometric curves of 2mg, 4mg, 6mg, 8mg and 10mg of OND with AMB.

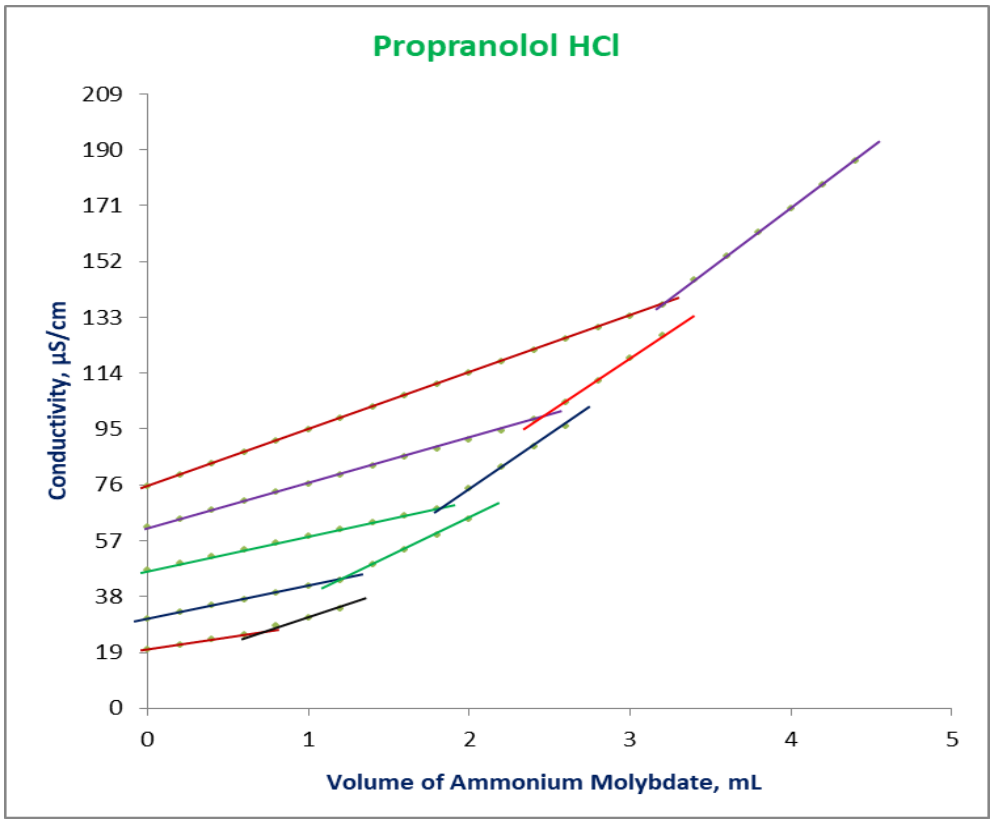

Fig.3. Conductometric curves of 2mg, 4mg, 6mg, 8mg and 10mg of PRP with AMB.

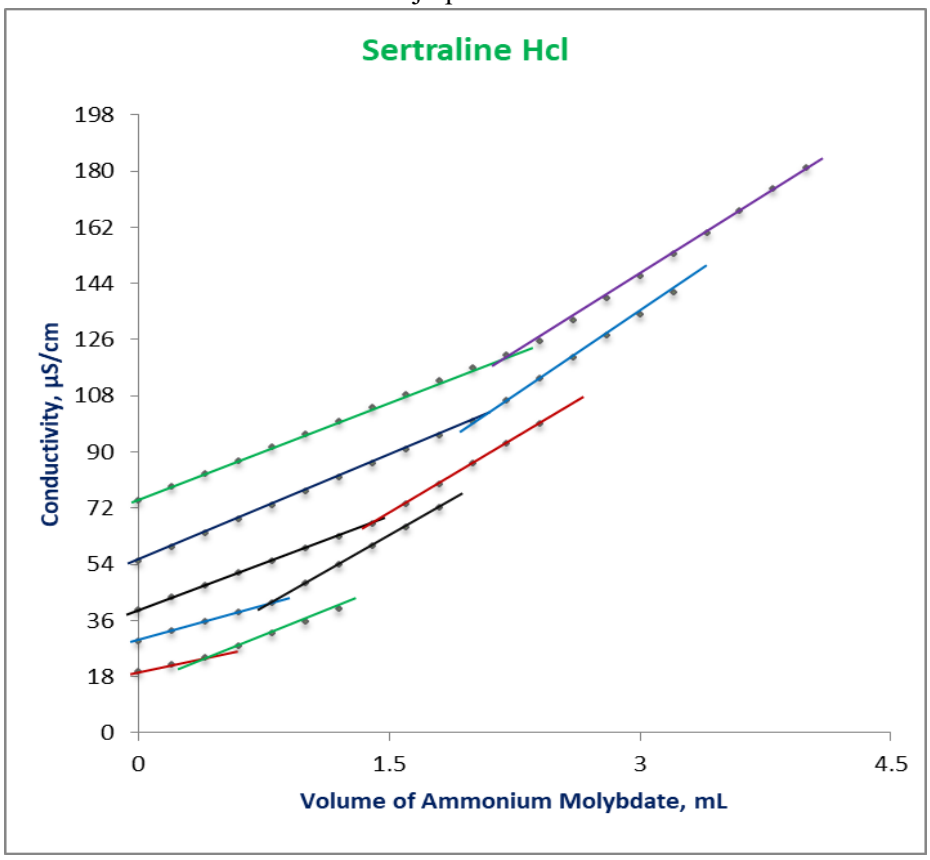

Fig.4.Conductometric curves of 2mg, 4mg, 6mg, 8mg and 10mg of SET with AMB.

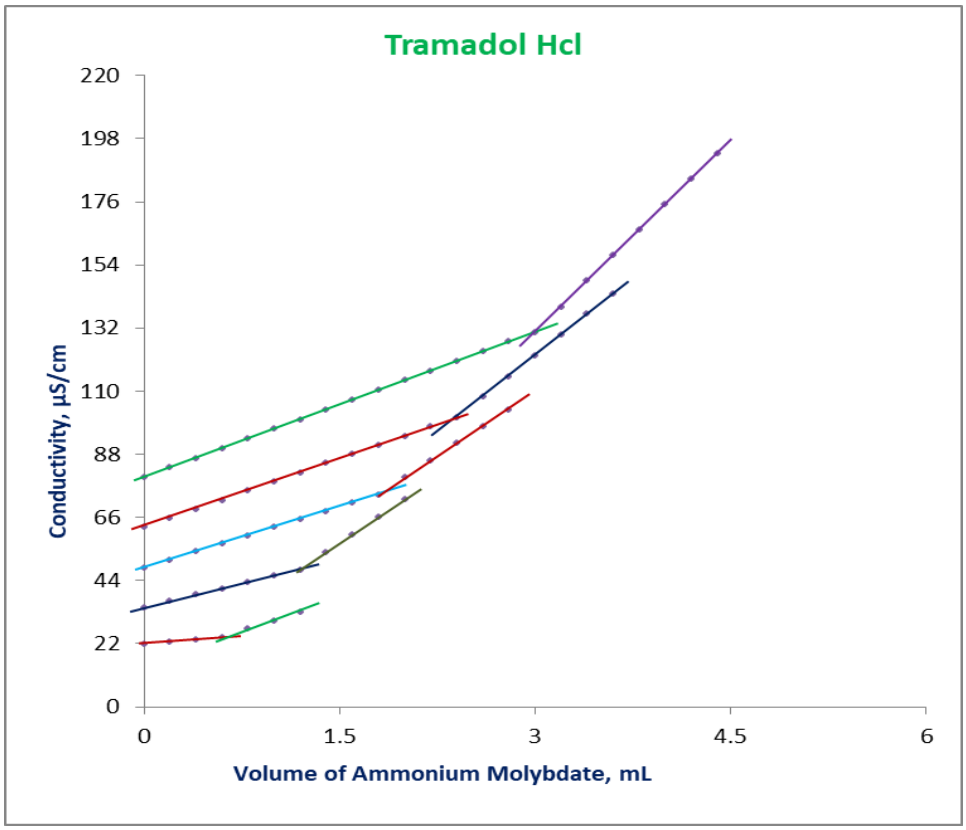

Fig.5. Conductometric curves of 2mg, 4mg, 6mg, 8mg and 10mg of TRM with AMB.

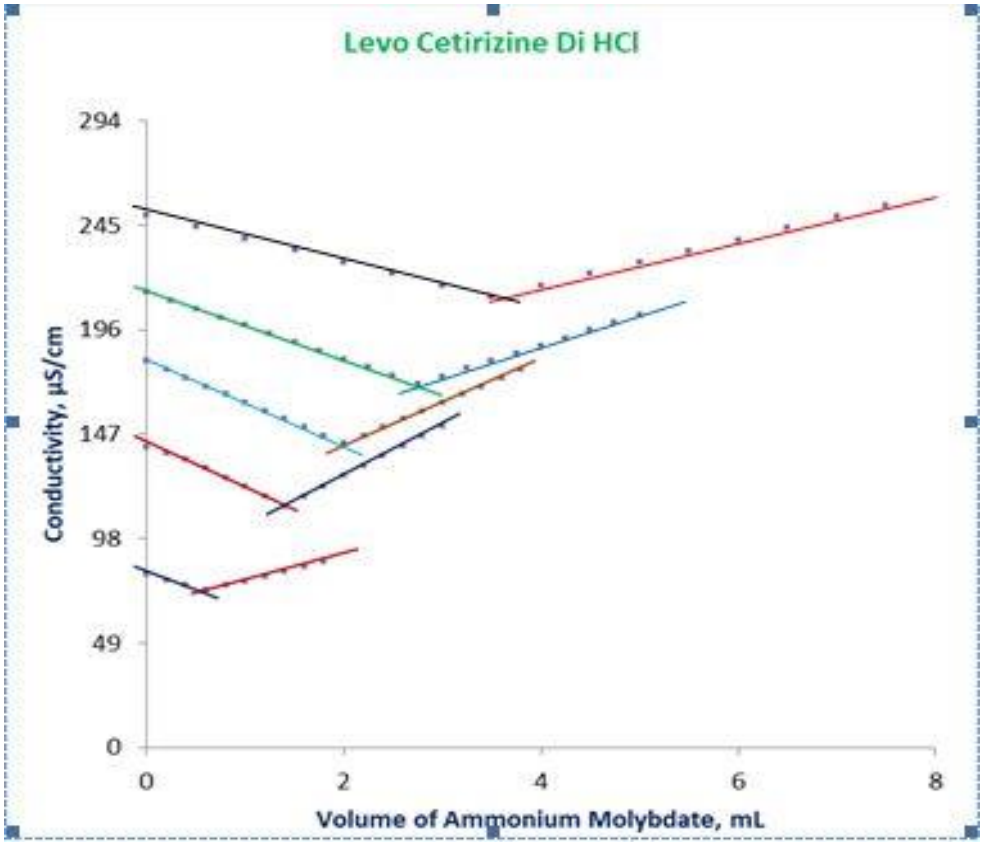

Fig.6. Conductometric curves of 2mg, 4mg, 6mg, 8mg and 10mg of LEV with AMB

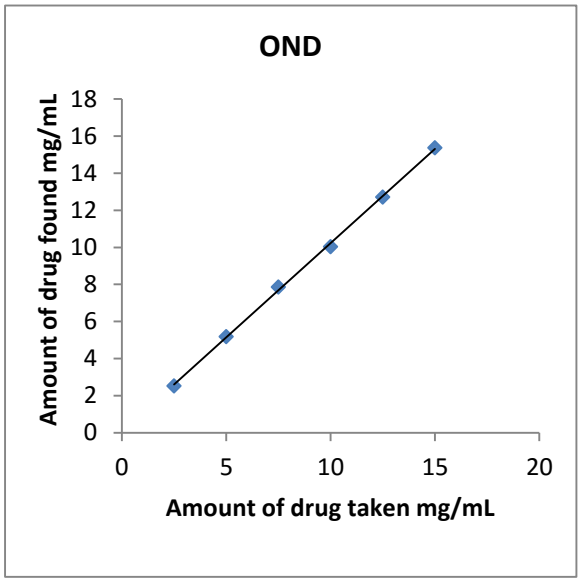

Fig.7a. Calibration graph of OND.

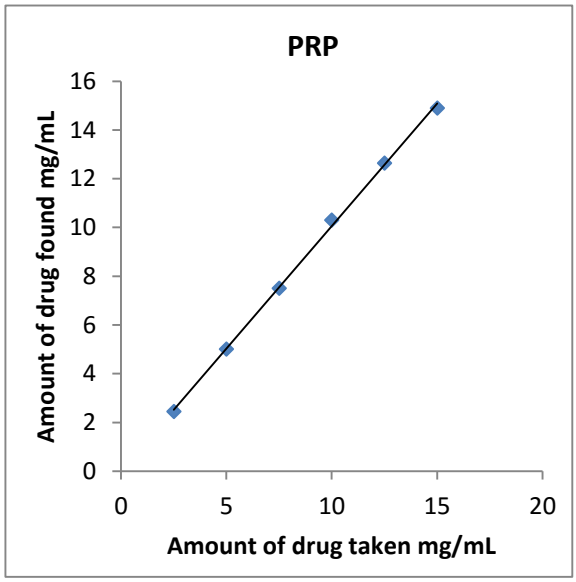

Fig.7b. Calibration graph of PRP.

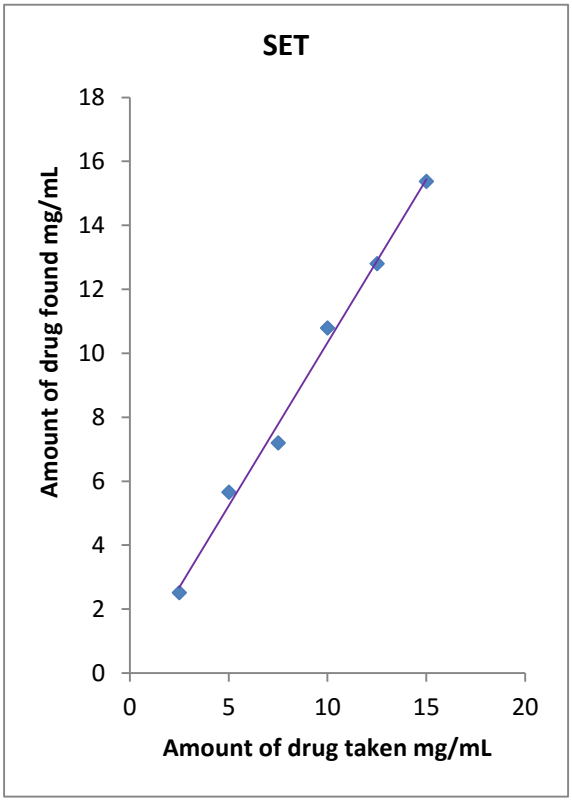

Fig .7c. Calibration graph of SET

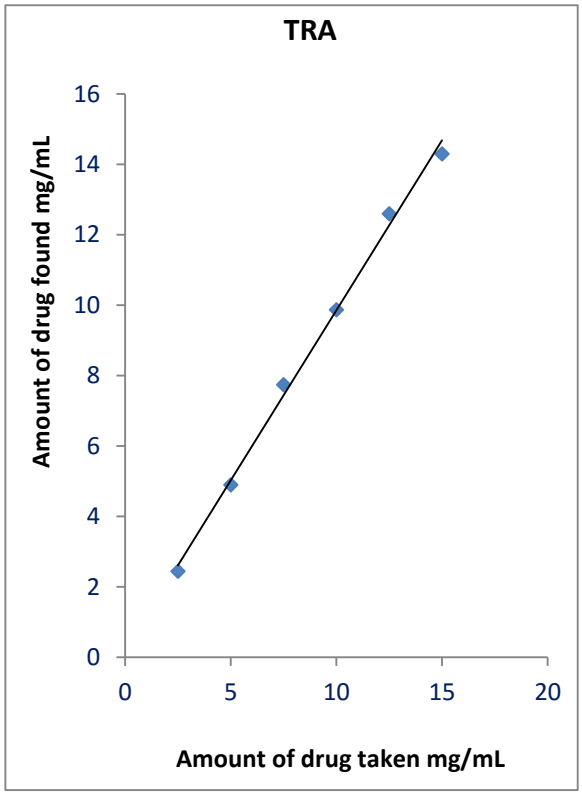

Fig.7d. Calibration graph of TRA.

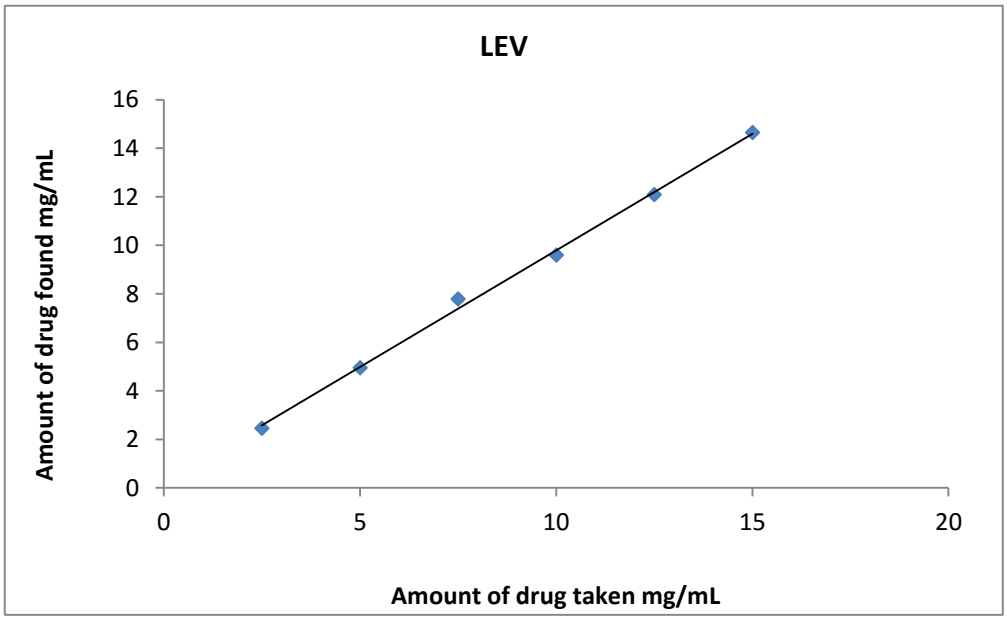

Fig.7e. Calibration graph of LEV.

Fig.7. Calibration graphs of Drugs

2.4. Optimization of the parameters of quantification

2.4.1. Effect of Solvent

Titrations in different solvents were performed to obtain the best results 1) Drug and reagent in ethanolic solution 2) Drug and reagent in acetone solution 3) Drug and reagent in methanol solution 4) Aqueous solutions of both drug and reagent. Preliminary experiments showed that procedure in aqueous media was the most suitable solvent for best results which gives higher conductance and most sharp endpoint.

2.4.2. Effect of reagent concentration

A fixed weight of investigated drugs were dissolved in 25 mL bi distilled water and titrated against $1x10^{-3}$, $1.5x10^{-3}$and $2.5x10^{-3}M$ Ammonium Molybdate solution. The results indicated that, titrant solutions lower than $2.5x10^{-3}M$ are not suitable for Conductometric titrations as the conductance readings were unstable, more time was needed to obtain constant conductance values and inflection at the end point was very poor. So, the reagent concentration must be not less than ten times that of the drug solution in order to minimize the dilution effect on the conductivity throughout the titration. The optimum concentration of Ammonium Molybdate is $2.5x10^{-3}M$ to get a highly stable conductance reading after 2 minutes of mixing.

2.4.3. Effect of Temperature

The experiment was performed at room temperature. The rise in temperature to 40^0C showed that the conductivity of the whole solution increases, as the temperature increases.

2.4.4. Linearity

In order to establish whether the proposed method exhibits any fixed or proportional bias, a simple linear regression of observed drug concentration against the volume of Ammonium Molybdate was calculated. Student's t-test (at 95% confidence level) was applied to the slope of the regression line and showed that it did not differ significantly from the ideal value of unity. The standard deviation (SD) can be considered satisfactory, at least for the level of concentrations examined [Table.3].

2.4.5. Accuracy and precision

To assess the precision, each experiment was repeated at least four times and accuracy is estimated in terms of percent recovery and percent RSD. Excellent per cent 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 their permissible range indicating high accuracy and precision of the methods (Table.4). LOD and LOQ can be determined for each drug [Table1&2].

2.5. Procedure for analysis of Pharmaceuticals

2.5.1. Ondansetron Hydrochloride

Twenty five tablets (Emeset 8 mg) were collected and crushed into powder. 150 mg equivalent of Ondansetron Hydrochloride was weighed from tablet powder and transferred into 150 mL

volumetric standard flask, completely dissolved in bi distilled water by sonication technique for 30 minutes and filtered with Eisco qualitative filter paper. After that the Solution converted to working concentration on dilution with bi distilled water for Conductometric titration of Ondansetron Hydrochloride solution with Ammonium Molybdate reagent.

2.5.2. Propranolol Hydrochloride

Twenty nine tablets Watson 8 mg were collected and crushed into powder. 150 mg equivalent of Propranolol Hydrochloride sodium was weighed from tablet powder and transferred into 150 mL volumetric standard flask, completely dissolved in bi distilled water by sonication technique for 30 minutes and filtered with Eisco qualitative filter paper. After that the Solution converted to working concentration on dilution with bi distilled water for Conductometric titration of Propranolol Hydrochloride solution with Ammonium Molybdate reagent.

2.5.3. Sertraline Hydrochloride

Ten tablets (Zolofit 25 mg) were collected and crushed into powder. 150 mg equivalent of Sertraline Hydrochloride was weighed from tablet powder and transferred into 150 mL volumetric standard flask, completely dissolved in bi distilled water by sonication technique for 30 minutes and filtered with Eisco qualitative filter paper. After that the Solution converted to working concentration on dilution with bi distilled water for Conductometric titration of Sertraline Hydrochloride solution with Ammonium Molybdate reagent.

2.5.4. Tramadol Hydrochloride

Five tablets (Tramal 50 mg) were collected and crushed into powder. 200 mg equivalent of Tramadol Hydrochloride was weighed from tablet powder and transferred into 200 mL volumetric standard flask, completely dissolved in bi distilled water by sonication technique for 30 minutes and filtered with Eisco qualitative filter paper. After that the Solution converted to working concentration on dilution with bi distilled water for Conductometric titration of Tramadol Hydrochloride solution with Ammonium Molybdate reagent.

2.5.5. Levo Cetirizine Di Hydrochloride

Two tablets of Levocis 500 mg were collected and crushed into powder. 200 mg equivalent of Levo Cetirizine Di Hydrochloride was weighed from tablet powder and transferred into 200 mL volumetric standard flask, completely dissolved in bi distilled water by sonication technique for 30 minutes and filtered with Eisco qualitative filter paper. After that the Solution converted to working concentration on dilution with bi distilled water for Conductometric titration of Levo Cetirizine Di Hydrochloride solution with Ammonium Molybdate reagent.

3. RESULTS AND DISCUSSION

Conductometric measurements can be used in quantitative precipitation titrations in which the conductance of the solution varies before and after the equivalence point, so that two intersecting lines can be drawn to indicate the end-point. On using Ammonium Molybdate as a titrant for the

determination of studied drugs, Drug Cation and Molybdate Anion is precipitated leading to a straight line during the first segment of the titration curve. The second segment of this curve corresponds to the excess of Ammonium Molybdate. To know the validity of the proposed method, a statistical analysis of the data obtained from its application on drugs in the pure form and in pharmaceutical formulations was performed. Results show that the proposed method is satisfactorily accurate, precise and reproducible over a concentration range of 2.5-15 mg for all the studied drugs.

Table 1: Conductometric determination of the drugs by Ammonium Molybdate as reagent and calculation of regression and analytical parameters

Name of the Drugs /Analytical Parameters	OND	PRP	SET	TRA	LEV
Concentration of drug mg/mL	2.5-15	2.5-15	2.5-15	2.5-15	2.5-15
Sandell's sensitivity(mg/cm^2)	0.00098	0.00099	0.00098	0.001	0.001
LOD mg/mL	0.006668	0.0085	0.0042	0.0044	0.0017
LOQ mg/mL	0.020	0.0257	0.0127	0.0134	0.0052
Slope, b	1.018	1.005	1.02	0.966	0.962
Intercept, a	0.0495	0.013	0.1268	0.195	0.173
Correlation co-efficient, R	9.99 x10^{-1}	0.999	9.93 x10^{-1}	0.996	9.98 x10^{-1}
Regression equation Y*	1.0177X + 4.95x10^{-2}	1.0048X + 1.3x10^{-2}	1.0204X + 1.268x10^{-1}	0.9658X + 1.949x10^{-1}	0.9619X+ 1.732x10^{-4}
SD of intercept (Sa)	7.1 x10^{-3}	5.7 x10^{-4}	9.6 x10^{-3}	5.2 x10^{-3}	7.2 x10^{-3}

Table 2: Precision and accuracy parameters evaluation by recovery studies method for quantitative determination of pure drugs by Conductometric titration with Ammonium. Molybdate

Name of the Drug Sample	Drug Taken (µg/mL)	Drug Found (µg/mL)	Percentage of Error	Percentage of drug Recovery	Regression SD of drug	Mean ± SD of Proposed method
OND	6	6.01	0.17	100.17	0.231	99.96±0.231
	12	11.98	0.17	99.83		
	13	12.96	0.31	99.69		
	15	15.02	0.1	100.13		
PRP	6	5.96	0.67	99.33	0.294	99.78±0.293
	9	8.89	1.22	98.78		
	10	9.96	0.4	99.6		
	12	12.02	0.17	100.17		

SET	7	6.98	0.29	99.7	0.448	99.71±0.447
	9	8.92	0.89	99.1		
	11	10.02	0.18	100.18		
	13	12.98	0.15	99.85		
TRM	8	8.01	0.2	100.2	0.227	99.88±0.226
	10	9.98	0.2	99.8		
	12	11.96	0.33	99.67		
	16	15.98	0.13	99.87		
LEV	5	4.92	1.6	98.4	0.849	99.92±0.846
	7	6.98	0.29	99.7		
	11	11.02	0.18	100.18		
	15	15.03	0.2	100.2		

Table 3: Precision, Accuracy evaluation by recovery studies method for quantitative determination of drugs by Conductometric titration with Ammonium Molybdate

Name of the Tablet Sample	**Drug Taken (µg/mL)**	**Drug Found (µg/mL)**	**%of Error**	**% of drug Recovery**	**Regression SD of drug**	**Mean± SD (Reference method)**	**Mean ± SD (Proposed method)**
OND (Emeset 8mg)	5	4.96	0.8	99.2	0.365	99.68± 0.364	99.54± 0.183
	10	9.98	0.2	99.8			
	12	11.96	0.33	99.67			
	14	14.01	0.07	100.07			
PRP (Watson 8 mg)	7	6.96	0.57	99.43	0.288	99.78± 0.288	98.61± 0.43
	10	9.98	0.2	99.8			
	9	8.98	0.22	99.78			
	15	15.02	0.13	100.13			
SET (Zoloft 25 mg)	6	5.96	0.67	99.33	0.344	99.69± 0.355	99.82±0.832
	8	7.96	0.5	99.5			
	10	10.01	0.1	100.1			
	13	12.98	0.15	99.85			
TRM (Tramal, 50 mg)	6	5.98	0.33	99.67	0.187	99.85± 0.186	99.76± 0.921
	9	9.01	0.11	100.1			
	12	11.98	0.17	99.83			
	15	14.97	0.2	99.8			

LEV (Levocis 50mg)	3	2.96	1.33	98.67	0.642	98.54± 0.640	98.54± 0.856
	6	5.97	0.5	99.5			
	10	10.01	0.1	99.9			
	14	13.99	0.07	99.93			

Table 4: Student's t-test and F-test evaluation by recovery studies method for quantitative determination of drugs

Tablets/ parameter	OND (Emeset -8mg)	PRP (Watson8 mg)	SET (Zoloft25 mg)	TRM (Tramal,50 mg)	LEV (Levocis 50mg)
t-test	1.92	0.677	1.32	1.913	0.49
F-test	0.04	0.464	0.04	0.041	0.557

4. CONCLUSION

The present study described the successful development of new, simple, sensitive, selective, accurate and rapid spectrophotometric method for the accurate determination of drugs each one in its pharmaceutical forms Ammonium Molybdate as precipitating 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 good alternative to the reported methods for the determination of these drugs.

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CONFLICT OF INETREST

Authors have no any conflict of interest.

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