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Titrimetric micro-determination of therapeutically active phenothiazines using periodate

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Abstract

Two new simple, accurate and precise titrimetric micro-procedures are described for the analysis of phenothiazines in pure sample, tablets, injections and syrup using periodate as the oxidant. The first method is based on the oxidation of phenothiazines with periodate in acid medium and the iodate formed in the reaction is determined by reacting it with iodide and titrating the liberated iodine with thiosulfate after masking the excess of periodate with molybdate. In the second procedure, the unreacted (excess) periodate is determined iodometrically under basic conditions. The reaction conditions have been optimised and the stoichiometry of the reaction has been evaluated. A linear relationship exists between the amount of the drug and the titration end-point as shown by the values of correlation coefficient, r (0.9991–0.9999). The slope of the linear relationship has been calculated and found to be in the range, 0.1457–0.3120. The methods were applied to the analysis of dosage forms with results comparable to those given by the official methods. Both the methods are indirect visual titration methods, and are simpler than, and superior to, many existing methods for the assay of phenothiazines.

Keywords: Titrimetry; Micro-determination; Phenothiazines; Periodate; Dosage forms

1. Introduction

N-substituted phenothiazine tranquillisers metabolise rapidly to give numerous products [1] of varying antipsychotic effectiveness [2]. Chlorpromazine, a dopamine inhibitor is the most commonly prescribed; others additionally possess antiemetic, antihistaminic, antiparkinson and other properties. Many techniques have been described in the literature for the determination of phenothiazines based on their reducing property and their ability to form coloured compounds. These methods have been reviewed [3–6].

The most widely used direct titrimetric methods are based on the oxidation of the heterocyclic S-atom to sulfoxide with acidic vanadate [7], dichromate [8], hexacyanoferrate(III) [9] and *N*-bromosuccinimide [10]. But these procedures require a very high acid concentration [7–10] for stoichiometric end-point and a screening indicator [9,10]. Several indirect redox titrimetric procedures have been suggested based on the use of chloramine-T [11], iodate [12], iodine monochloride [13], bromine monochloride [14], *N*-bromosuccinimide [15], 1-chlorobenzotriazole [16] and sodium chlorite [17]. Methods employing chloramine-T and iodine monochloride use a large volume of concentrated hydrochloric acid (Andrew's procedure), and are applicable to semi-micro samples only. The *N*-bromosuccinimide method requires strict adherence to the standing time of 30–90 min beyond which time the analysis suffers from lack of stoichiometry due to nuclear bromination of the aromatic moiety. The other methods suffer from the disadvantages of instability of the reagent [16], insufficient accuracy and sensitivity [17], critical reaction conditions [14] where the reaction is to be carried out at 0–4 °C.

Titrimetric methods based on the reaction with metal ions have also been reported. Phenothiazines have been determined with picrates of lead and zinc [18,19], tetraiodobismuthate [20], tetraiodoplumbite [21] and mercuric chloride [22]. The procedures involve precipitation, filtration and titration of excess metal with EDTA, and are therefore complex, time-consuming and are not readily applicable to routine analysis.

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In addition, they are not of general applicability and are adversely affected by the appreciable solubility of the precipitate, and are not suitable for micro-scale determination.

The present investigation was undertaken with the aim of developing new, simple, rapid and accurate methods free from many shortcomings that are usually encountered in other titrimetric methods. In this work, the oxidation of phenothiazines with periodate has been investigated and used to develop two titrimetric procedures. In one method (Method A), the periodate left after the reaction with phenothiazines was determined by reaction with an excess of iodide at pH 8.5 and the liberated iodine was titrated with thiosulfate. In the other (Method B), the excess periodate was masked with molybdate at pH 3 to form the heteropoly acid, 6-molybdo-1-periodic acid. Under these conditions, iodate formed in the reaction between phenothiazine and periodate is not masked, and the liberated iodine from iodide was titrated with thiosulfate.

2. Experimental

2.1. Reagents and solutions

All chemicals used were of analytical reagent grade and double distilled water was always used in the study. A stock solution of sodium periodate (0.02 M) was prepared by dissolving 4.28 g of reagent (Sd. Fine Chem., India) in water and diluting to 1 l. It was diluted to 0.01 M for Method B. A 0.01 M stock solution of sodium thiosulfate was prepared by dissolving 2.48 g of the reagent (Sisco Chem. India Ltd.) in water and diluting to 1 l. This was suitably diluted to get 0.005 M solution and standardised with potassium iodate solution of equivalent strength. The buffer solution of pH 3 was prepared by dissolving 25 g monochloroacetic acid (Merck) in 70 ml of distilled water and adjusting the pH to 3, with a pH meter, by adding strong sodium hydroxide solution. Politzsch buffer of pH 8.5 was prepared by mixing equal volumes of 0.2 M boric acid (Sisco Chem. India Ltd.) and 0.05 M borax (Sarabhai Chemicals, India). A 1% solution of starch indicator (Bangalore Pharm. Res. Lab.), aqueous solutions of 10% ammonium molybdate (Glaxo Chem. India, Ltd.), 10% potassium iodide (Indian Drugs and Pharmaceuticals Ltd.) and 1:1 ammonia (Sd. Fine Chem., India) were prepared in the usual way. A 10 M solution of sulfuric acid was prepared by adding 556 ml of concentrated acid (Qualigens India Ltd.), specific gravity 1.84, to 446 ml of water with cooling.

2.1.1. Standard drug solutions

Pharmaceutical grade phenothiazines were kindly given by various pharmaceutical companies and were used as received. Stock standard solutions of phenothiazines, 2 mg/ml, were prepared by dissolving 200 mg each of chlorpromazine hydrochloride, CPH (British Pharm. India Ltd.), promethazine hydrochloride, PH, prochlorperazine maleate, PCPM, and prochlorperazine mesylate, PCPMS (Rhone–Poulenc India, Ltd.), thioridazine hydrochloride, TH (Sandoz India Ltd.) or trifluoperazine hydrochloride, TFPH (SmithKline Beecham, India Ltd.) in water and diluting to 100 ml in a volumetric flask (in the case of PCPM, a few drops of 0.1 M HCl were used to aid dissolution before diluting to the mark). The solutions were stored in amber-coloured bottles and kept in a refrigerator. Working solutions were prepared by appropriate dilution before use.

2.2. Procedures

2.2.1. Method A

A 10 ml aliquot of solution containing 1–10 mg of CPH or TH, 2–10 mg of PH, 2–20 mg of PCPM, 2–16 mg TFPH or 2–18 mg of PCPMS was placed in a 100 ml Erlenmeyer flask; this was followed by the addition of 2 ml H_2SO_4 (10 M) and 5 ml $NaIO_4$ (0.02 M) and the contents were swirled and allowed to stand for specified time (Table 1) at room temperature for the oxidation of the drugs to complete as indicated by the complete disappearance of the orange, red, reddish-violet or blue colour due to the phenothiazonium radical cation. Freshly prepared 1:1 ammonia solution ($\sim$7.5 ml) was added to raise the pH to $\sim$8.5 followed by 5 ml of Politzsch buffer and 5 ml of 10% potassium iodide. The flask was again left for about 10 min and the liberated iodine was titrated with 0.005 M thiosulfate, 1 ml of 1% starch solution being added near the end-point. The whole procedure was applied in a blank determination on water.

2.2.2. Method B

A 10 ml aliquot of drug solution containing 0.2–2.0 mg of CPH or PH, 0.3–3.6 mg of TH and 0.4–4.0 mg of PCPM, PCPMS or TFPH was transferred by means of a pipette into a 100 ml Erlenmeyer flask. The solution was acidified by adding 1 ml of H_2SO_4 (10 M) followed by the addition of 5 ml of $NaIO_4$ (0.01 M) solution. The contents were swirled and set aside for 5–20 min, depending on the individual phenothiazine (Table 1), with occasional shaking to facilitate the oxidation of the drugs to respective sulfoxides. Freshly prepared 10% ammonium molybdate solution (10 ml), 10 ml of chloroacetate buffer solution and 10% (5 ml) potassium iodide solution were added, and the flask was again left for 1 min. The liberated iodine was titrated with 0.005 M thiosulfate to a starch end-point. A blank experiment was carried out without phenothiazine drug. In either method, the amount of drug was calculated using the equation:

Table 1
Reaction stoichiometry, reaction time, range of determination and correlation coefficient

Phenothiazine drug	Method A						Method B					
	Stoichiometry [a]		Reaction time (min)	Range (mg)	Slope	r [b]	Stoichiometry [a]		Reaction time (min)	Range (mg)	Slope	r [b]
	Amount taken (mg)	n [c]					Amount taken (mg)	n [c]				
CPH	4.0	2.01	15	1–10	0.2830	0.9997	0.4	1.02	15	0.2–2.0	0.2792	0.9995
	7.0	2.01					0.8	1.01				
	10.0	2.00					1.2	0.92				
PH	2.0	2.05	10	2–10	0.3093	0.9999	0.4	0.97	10	0.2–2.0	0.3120	0.9996
	4.0	2.00					0.8	0.98				
	8.0	2.01					1.2	0.99				
TH	1.0	1.92	10	1–10	0.2465	0.9992	0.6	0.99	15	0.3–3.6	0.2447	0.9999
	4.0	2.00					1.2	1.01				
	7.0	2.01					1.8	0.98				
PCPMS	4.0	1.97	15	2–18	0.1457	0.9998	0.8	0.93	20	0.4–4.0	0.1470	0.9991
	8.0	1.99					2.0	0.99				
	12.0	2.01					3.2	1.02				
PCPM	8.0	1.95	20	2–20	0.1625	0.9998	1.6	1.02	15	0.4–4.0	0.1484	0.9999
	12.0	1.97					2.4	0.99				
	16.0	1.98					3.2	1.01				
TFPH	6.0	1.95	25	2–16	0.2102	0.9999	0.8	1.02	20	0.4–4.0	0.2045	0.9998
	8.0	1.98					1.6	1.01				
	12.0	1.97					3.6	0.99				

[a] Average of three determinations.
[b] r: Correlation coefficient.
[c] n: Number of moles of oxidant consumed per mole of drug.

$$\text{Amount of drug (mg)} = \frac{VMR}{n}$$

where V = volume of periodate consumed by the drug (ml), M = molecular weight of the drug, R = molarity of periodate solution, and n = number of moles of periodate reacting with 1 mol of drug.

2.3. Determination of phenothiazines in dosage forms

2.3.1. Tablets

Depending on the drug content per tablet, 20–80 tablets were weighed accurately and ground into a fine powder. An amount of the powder equivalent to 200 mg of active component was weighed into a 100 ml standard flask, about 60 ml water was added and the contents were shaken thoroughly for about 20 min. In the case of stemetil tablets (PCPM), a few drops of 0.1 M HCl were used to aid extraction of drug. Then, the volume was made up to the mark, mixed well and filtered. The filtrate was diluted appropriately and a 10 ml aliquot was used for assay.

2.3.2. Injections

The contents of 20 ampoules were mixed well and an accurately measured volume equivalent to 200 mg of the drug was diluted to 100 ml with distilled water in a volumetric flask and mixed well. Then, the steps described for tablets were followed. The same samples were assayed by the BP methods also [31] for comparison and the results are presented in Table 6.

3. Results and discussion

The methods presented are based on the oxidation of phenothiazine drugs quantitatively to respective sulfoxides by periodate in sulfuric acid medium and subsequent determination of residual periodate (Method A) or iodate formed by the reduction of periodate (Method B), iodometrically. The periodate or iodate, so determined, was a quantitative measure of the amount of phenothiazine drug.

Oxidative titrimetric determination of many pharmaceutically important substances including nucleic acids [23], mannitol [24], ionositol [25], penicillins [26], riboflavine [27], mandelic acid [28], nadolol [29] and biotin [30] has been achieved with periodate. In the present investigation, periodate was found to react quantitatively with phenothiazines first to form the coloured radical cation, and subsequently, the colourless sulfoxide. A study of the stoichiometry of the reaction between periodate and phenothiazines showed that 2 and 1 mol of periodate were required for oxidation in Methods A and B, respectively. The probable explanation for the difference in the number of moles of oxidant reacting with each mole of drug is that in Method A, the oxidation of the drugs will occur in acidic condition and the titration of the residual periodate will be completed in alkaline conditions.

3.1. Optimisation of experimental conditions

The first step in the assay procedures is the oxidation of phenothiazines to respective sulfoxides as indicated by the complete disappearance of orange, red, reddish-violet or blue colour of the phenothiazonium radial cation which will be complete in 10–25 min. This was achieved by excess of oxidant, 0.02 and 0.01 M sodium periodate (5 ml) in the presence of 2 and 1 ml of 10 M H_2SO_4 in a total volume of 15 ml, in Methods A and B, respectively. The reaction was found to be quantitative in the specified oxidant and acidic conditions. The reaction time could be reduced by employing higher acidic conditions, but that was seldom done so that excessive amounts of ammonia would not be required for later neutralisation.

After the oxidation was complete, about 7.5 and 3.0 ml of 1:1 ammonia were required to neutralise the acid and to raise the pH to required level, in Methods A and B, respectively. A 5 ml volume of Politzsch buffer (Method A) and 10 ml of monochloroacetate buffer (Method B) were found to be optimum for adjusting and maintaining the pH 8.5 and 3, respectively. To react quantitatively with the residual periodate (Method A) or with iodate formed in the reaction between phenothiazines and periodate (Method B) which was taken as a measure of the amount of phenothiazine drug, 5 ml potassium iodide solution (10%) was found adequate. In Method B, the iodate formed by the reduction of periodate was determined after masking the latter with 10 ml ammonium molybdate (10%). The liberation of iodine by residual periodate and iodate formed was complete in 10 and 1 min, respectively, at the specified pH.

The relationship between the titration end-points obtained by the proposed methods and the drug amounts was examined. The linearity between the amount of the drug and titration end-point is apparent from the correlation coefficient. The correlation coefficients of 0.9992–0.9999 (Method A) and of 0.9991 to 0.9999 (Method B) show that the reaction between periodate and the studied drugs proceeds stoichiometrically in a molar ratio of 2:1 and 1:1 in Methods A and B, respectively. The slope of the linear relationship is found to be in the range 0.1457–0.3093 and 0.1470–0.3120 for Methods A and B, respectively.

3.2. Range of determination

The minimum and maximum amounts of each drug that could be determined by the methods are given in Table 1. Below the lower limits indicated, quantitative results were not obtained and above the upper limits, reaction time increased.

3.3. Accuracy and precision, and ruggedness

In order to evaluate the accuracy of the method, pure drugs in different levels (within the working limits) were analysed by the methods proposed. The results for three levels of each drug are given in Tables 2 and 3. The precision of the method was ascertained by determining the relative standard deviation (RSD) of seven replicate analyses on the same solution containing the drugs in three levels. The error, range of error and RSD obtained are presented in Tables 2 and 3.

Table 2
Results of titrimetric determination of pure drugs using Method A

Drug	Amount taken (mg)	Amount found [a] (mg)	Range (mg)	Error (%)	Standard deviation (mg)	RSD [b] (%, $n = 7$)	Range of error (%)
CPH	3.0	2.94	0.22	2.00	0.09	3.05	3.04
	6.0	5.98	0.21	0.33	0.08	1.44	1.43
	10.0	10.09	0.32	0.90	0.12	1.23	1.22
PH	2.0	2.05	0.18	2.50	0.07	3.58	3.57
	6.0	5.94	0.16	1.00	0.06	1.05	1.04
	10.0	10.06	0.18	0.60	0.08	0.80	0.79
TH	3.0	3.11	0.36	3.66	0.14	4.68	4.67
	5.0	5.06	0.24	1.20	0.11	2.13	2.12
	8.0	8.06	0.36	0.75	0.13	1.72	1.71
PCPMS	6.0	6.07	0.40	1.16	0.13	2.27	2.26
	10.0	10.11	0.41	1.10	0.14	1.40	1.39
	14.0	13.86	0.36	1.00	0.15	1.09	1.08
PCPM	4.0	3.91	0.35	2.25	0.14	3.66	3.65
	10.0	9.82	0.18	1.80	0.12	1.26	1.25
	14.0	13.82	0.36	1.28	0.14	1.02	1.01
TFPH	6.0	5.91	0.28	1.50	0.09	1.63	1.62
	10.0	10.11	0.42	1.10	0.15	1.50	1.49
	14.0	13.88	0.28	0.85	0.10	0.76	0.75

[a] Average of seven determinations.
[b] RSD: relative standard deviation.

Table 3
Results of titrimetric determination of pure drugs using Method B

Drug	Amount taken (mg)	Amount found [a] (mg)	Range (mg)	Error (%)	Standard deviation (mg)	RSD (%, $n = 7$)	Range of error (%)
CPH	0.4	0.41	0.03	2.50	0.0158	3.85	3.84
	1.0	0.98	0.04	2.00	0.0156	1.59	1.59
	1.6	1.59	0.04	0.62	0.0195	1.23	1.23
PH	0.6	0.59	0.03	1.66	0.0129	2.18	2.18
	1.2	1.19	0.04	0.83	0.0173	1.45	1.45
	1.8	1.82	0.05	1.11	0.0141	0.77	0.77
TH	0.6	0.58	0.05	3.33	0.0191	3.30	3.29
	1.5	1.53	0.06	2.00	0.0208	1.36	1.36
	2.4	2.37	0.08	1.25	0.0297	1.25	1.25
PCPMS	0.8	0.78	0.08	2.50	0.0267	3.43	3.42
	1.6	1.63	0.06	1.87	0.0227	1.39	1.39
	2.4	2.36	0.09	1.66	0.0324	1.37	1.37
PCPM	1.2	1.22	0.05	1.66	0.0248	2.03	2.03
	2.0	1.96	0.08	2.01	0.0308	1.57	1.57
	2.8	2.84	0.08	1.43	0.0318	1.12	1.12
TFPH	1.6	1.62	0.06	1.25	0.0231	1.42	1.42
	2.0	1.97	0.09	1.50	0.0297	1.51	1.50
	3.2	3.16	0.09	1.25	0.0360	1.14	1.13

[a] Average of seven determinations.

Table 4
Between-day precision of the determination of phenothiazines by the proposed methods

Drug	Method A			Method B		
	Amount taken (mg)	Found (mg)	RSD (%) ($n = 4$)	Amount taken (mg)	Found (mg)	RSD (%) ($n = 4$)
CPH	3	2.91	3.62	0.4	0.41	5.07
	5	4.94	1.73	1.0	0.98	1.31
	8	7.93	0.72	1.6	1.59	1.25
PH	4	4.03	2.14	0.6	0.59	1.38
	6	5.92	0.88	1.0	0.99	1.54
	8	7.88	0.66	1.6	1.58	0.63
TH	4	4.03	1.71	0.9	0.88	0.92
	6	5.90	1.66	1.8	1.82	0.63
	8	7.85	1.46	2.4	2.38	1.11
PCPMS	6	5.95	1.94	0.8	0.79	3.79
	8	8.07	2.07	2.0	1.98	1.23
	12	11.70	1.37	3.2	3.22	0.76
PCPM	8	7.84	1.87	1.6	1.57	1.91
	12	12.07	1.39	2.4	2.41	1.01
	16	15.86	0.92	3.2	3.21	0.89
TFPH	6	5.90	2.22	1.6	1.63	1.22
	8	7.98	1.01	2.0	1.96	1.31
	16	15.92	0.84	3.2	3.15	0.81

To prove the validity and applicability of the proposed methods, four replicate determinations at different concentration levels of each drug were carried out. The within-day RSD values were within 2%. The values of between-day RSD for different concentrations of each drug, obtained from determinations carried out over a period of 4 days are given in Table 4 and indicate that the proposed methods are highly reproducible.

3.4. Recovery experiments

To ascertain the validity of the methods, recovery experiments were performed. Known amounts of pure drug in three levels were added to a fixed amount of the same drug in the formulation previously analysed, and the total amount of the drug was determined by the proposed methods. The amount of pure drug added in each instance was then found by the difference. The results of this study summarised in Table 5 indicate that the end-point was unaffected by the presence of concomitant substances normally associated with the drugs in the formulations.

3.5. Application to formulations

The proposed procedures were applied to the determination of studied drugs in different formulations. Table 6 shows the percentage recoveries obtained by the proposed methods and the labelled amount. The RSDs are lower than 2%, indicating good precision and independence of the matrix effect over the end-point detection. The formulations were also analysed simultaneously by the BP methods [31]. The performance of the proposed methods was assessed by calculation of t- and F-values. At 95% confidence level, the calculated t- and F-values did not exceed the tabulated values. Hence, it can be concluded that there is no significant difference between the proposed methods and the official (reference) methods in terms of accuracy and precision.

3.6. Conclusions

The methods presented are simple, fast, and accurate and precise. They are considerably more sensitive than many similar methods cited in the literature. In fact, Method B is the most sensitive titrimetric method ever reported for the assay of phenothiazines. Moreover, the reagent used is superior to many reagents previously used because it is available as an analytical grade reagent, has high molecular mass and is extremely stable, and can be used in both alkaline and acidic media.

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Table 5
Recovery studies by the standard addition method using the proposed methods

Drug	Formulation	Method A				Method B			
		Amount of drug present in the sample taken (mg)	Amount of pure drug added (mg)	Amount of pure drug found (mg)	Recovery [a] (%)	Amount of drug present in the sample taken (mg)	Amount of pure drug added (mg)	Amount of pure drug found (mg)	Recovery [a] (%)
CPH	CPH tablets (25 mg)	2.01	4	3.98	99.5	0.398	0.6	0.61	101.6
		2.01	6	5.89	98.2	0.398	1.0	0.98	98.0
		2.01	8	8.09	101.1	0.398	1.4	1.38	98.5
	Megatil injections (25 mg)	1.99	4	4.10	102.5	0.401	0.6	0.59	98.3
		1.99	6	6.08	101.3	0.401	1.0	1.01	101.0
		1.99	8	7.88	98.5	0.401	1.4	1.39	99.2
PH	Phenergan tablets (10 mg)	1.98	4	4.01	100.2	0.403	0.6	0.58	96.6
		1.98	6	5.97	99.5	0.403	1.0	0.99	99.0
		1.98	8	7.84	98.0	0.403	1.4	1.38	98.5
	Phenergan injections (25 mg)	1.96	4	3.92	98.0	0.396	0.6	0.62	103.3
		1.96	6	6.15	102.5	0.396	1.0	1.00	100.1
		1.96	8	7.93	99.1	0.396	1.4	1.39	99.2
TH	Ridazine tablets (50 mg)	2.02	4	3.97	99.2	0.605	1.2	1.19	99.1
		2.02	6	5.90	98.3	0.605	1.8	1.76	97.7
		2.02	8	7.94	99.3	0.605	2.4	2.42	100.8
PCPMS	Stemetil injections (12.5 mg)	3.98	6	6.05	100.9	0.798	1.6	1.62	101.2
		3.98	8	7.86	98.25	0.798	2.0	1.98	99.0
		3.98	10	10.28	102.8	0.798	2.4	2.45	102.2
PCPM	Stemetil tablets (5 mg)	3.98	6	5.88	98.0	0.804	1.6	1.65	103.4
		3.98	8	7.84	98.1	0.804	2.0	1.96	98.4
		3.98	10	9.92	99.2	0.804	2.4	2.36	98.5
TFPH	Trazine tablets (5 mg)	3.93	6	5.88	98.1	0.794	1.6	1.58	98.9
		3.93	8	7.95	99.3	0.794	2.0	1.95	97.8
		3.93	10	10.11	101.1	0.794	2.4	2.43	101.4

[a] Average of three determinations.

Table 6
Results of assay of pharmaceutical formulations by the proposed methods

Drug and its formulation	Label claim (mg/tablet or mg/ml)	Found [a] (% Recovery ± SD)			Student's *t*-value [b]		*F*-value [c]	
		Method A	Method B	Official BP method	Method A	Method B	Method A	Method B
CPH								
CPH tablets [d]	25	100.23 ± 0.86	99.64 ± 0.96	99.20 ± 1.26	1.53	0.62	2.14	1.72
Megatil tablets [e]	50	98.10 ± 1.14	99.35 ± 0.28	99.80 ± 0.50	3.27	1.82	5.19	3.18
Megatil injections [e]	25	99.68 ± 1.02	100.36 ± 0.88	100.24 ± 0.74	1.00	0.23	1.99	1.41
PH								
Phenergan tablets [f]	10	98.40 ± 0.62	100.80 ± 0.48	99.60 ± 0.72	2.83	2.74	1.35	2.25
Phena tablets [g]	25	98.95 ± 0.26	99.28 ± 0.62	99.56 ± 0.56	2.35	0.65	4.63	1.22
Phenergan injections [f]	25	98.16 ± 1.32	99.15 ± 0.85	98.32 ± 0.70	0.25	1.69	3.55	1.47
TH								
Melleril tablets [h]	10	97.80 ± 1.14	101.05 ± 1.22	98.50 ± 0.84	1.12	2.14	1.84	2.10
Ridazine tablets [d]	50	100.74 ± 1.28	100.85 ± 0.70	102.00 ± 0.96	1.77	2.19	1.77	1.88
Tensaril tablets [i]	200	99.38 ± 0.86	98.30 ± 1.42	99.20 ± 0.64	0.38	1.38	1.80	4.92
PCPMS								
Stemetil injections [f]	12.5	99.60 ± 1.18	99.82 ± 0.76	99.52 ± 0.72	0.11	0.64	2.68	1.11
PCPM								
Stemetil tablets [f]	5	99.58 ± 0.54	100.60 ± 0.92	100.40 ± 0.89	1.81	0.28	2.71	1.42
Emidoxyn tablets [j]	5	101.06 ± 0.38	100.80 ± 0.92	100.60 ± 0.72	1.32	0.33	3.59	1.68
TFPH								
Neocalm tablets [e]	5	98.14 ± 0.73	98.66 ± 0.83	99.13 ± 1.02	1.78	0.80	1.83	1.51
Trazine tablets [d]	5	98.38 ± 1.62	99.37 ± 0.57	100.02 ± 0.81	2.13	1.48	4.00	2.02

[a] Average of five determinations ± standard deviation.
[b] Tabulated *t*-value at 95% confidence level is 2.78.
[c] Tabulated *F*-value at 95% confidence level is 6.39.
[d] Marketed by Sun Pharma.
[e] Marketed by Intas.
[f] Marketed by Rhone–Poulenc.
[g] Marketed by Ind-Swift.
[h] Marketed by Sandoz.
[i] Marketed by LA Pharma.
[j] Marketed by Rallis.

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