A Highly Sensitive Flame Emission Spectrophotometric Method for the Determination of some Phenothiazine Antipsychotics via Potassium Dichromate as Oxidant Reagent

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Abstract:

A flame emission method here is described for the determination of phenothiazines. The method based on the oxidation of phenothiazines in an acid medium to colorless sulfoxides via orange or purple-colored intermediates. In the begin employs flame emission spectrophotometric potassium intensity detection. The proposed method was successfully applied to the determination of phenothiazine in pharmaceutical preparations. The reliability of the assay was established by parallel determination by the official methods of British Pharmacopoeia.

The optimum reaction conditions and other analytical parameters are evaluated.

الخلاصة:

تم وصف طريقة طيفية لهبية لتقدير الفينوثايزينات. تعتمد الطريقة علـــى اكســـدة الفينوثايزينات في وسط حامضي الى السفوكسيدات العديمة اللون مقارنة بالمواد الوسطية ذات الالوان البرتقالية والوردية، واعتماداً على شدة انبعاث البوتاسيوم باستخدام مطيافيـــة الانبعاث اللهبي. طبقت الطريقة بنجاح فـــي تقـــدير الفينوثايزينـــات فـــي مستحضـــراته الصيدلانية، وتم تثبيت ظروف التفاعل المثلى والنتائج التحليلية.

Introduction:

Antipsychotic drugs have revolutionized the management of major psychiatric disorders and the outeomes of those who suffer from them. Phenothiazines which were introduced in the treatment of moderate to severe mental illnesses including schizophrenia. Phenothiazines also possess antiemetic, sedative, antipruritic, antidyskinetic, analygesic and antihistaminic properties[1]. the therapeutic importance of these drugs has prompted many workers to develop methods for their determination in body fluids as well as pharmaceuticals and these methods have been reviewed[2-4]. Many direct spectrophotometric methods for the determinations of phenothiazines have been suggested based on the oxidation of the drugs to the radical cations and subsequent measurement of absorbance, with use of such oxidizing agents as molybdate[5], iodate[6], bromate[7], Vanadate[8], N-bromosuccinimide[9], cerium(IV)[10], iron(III)[11], 2-iodobenzoate[12], and p-benzoquimone[13]. Some of these methods, unfortunately, suffer from several disadvantages like use of heating step[5], low sensitivity[10][11], very strong acid medium[9][13], low range of determination and critical working conditions[6-8] and poor selectivity. In this paper, we present the optimum conditions for the indirect flame emission spectrophotometric determination of phenothiazines with potassium dichromate. This new procedure is accurate, highly sensitive, rapid and simple. Atomic emission spectroscopy employing flames (also called flame emission spectroscopy or flame photometry) has found wide spread application to elemental analysis. Its most important uses have been in the determination of sodium, potassium, lithium, and calcium, particularly in biological fluids and tissues. For reasons of convenience, speed, and relative freedom has interferences, flame emission spectroscopy has become the method of choice for these otherwise difficult-to-determine elements. The method has also been applied, with varying degrees of success to the determination of perhaps half the elements in the periodic table[14].

The present communication reports the reaction of potassium dichromate to the determination of phenothiazine. The proposed method is simple, selective, rapid, free from various common interfering dosage form, and does not require extraction, close control of pH or heating steps.

In this work, a flame emission spectrophotometric method for the determination of phenothiazines are proposed and is based on its oxidation by potassium dichromate and then determination of the potassium ion content of the potassium dichromate. The proposed method was applied to determine the phenothiazines in its drug formulations including tablet and injection and satisfactory results were obtained in comparison with official method.

Experimental:

Apparatus: Flame emission spectrophotometer (Cornin G400).

Reagents: All chemicals used were of analytical reagent grade and phenothaizines standard material were provided from state company for drug industries and medical appliance (SDI) Sammara-Iraq.

Phenothiazines (1000µg/ml):

A stock standard solutions containing 1000µg/ml drug were prepared by dissolving a weighed amount of chloropromazine hydrochloride, CPH; Trifluoroperazine dihydrochloride, TFPH in distilled water.

The solutions were kept in an amber-colored bottle and stored refrigerator. Working solutions were prepared daily by appropriate dilution of the stock solution with distilled water.

Potassium dichromate (0.003 $mol.l^{-1}$):

Prepared by dissolving 0.8825gm potassium dichromate in 1000ml of distilled water.

Sulphuric Acid (10 $mol.l^{-1}$):

140ml of concentrated sulphuric acid (Sp.gr. 1.84) was diluted to 250ml with distilled water.

Adapted Procedure:

After a 5.0ml aliquot of phenothaizine drug solution containing 1-10mg CPH, 1-9mg TFPH was transferred into a 100ml conical flask and 10ml of 10$mol.l^{-1}$ sulfuric acid was added. The dichromate solution (0.003$mol.l^{-1}$) was added slowly from a 10ml burette with continuous stirring by a magnetic stirrer. At first, a purple color developed, and the titration was continued until the color completely disappeared after that the intensity of potassium was measured against a reagent blank. Based on the intensity of potassium, the amount of the drug was calculated.

Procedure for Assay of phenothiazine drug in Pharmaceutical Preparations:

Tablets: Twenty tablets (Labeled to contain 5mg of phenothiazine)were weighed and ground into a fine powder. An a mount of powder equivalent to about 200mg of the pure drug was weighed. The powder was extracted with three 30ml portions of water and filtered into a 100ml volumetric flask.

The filtrated was washed and diluted to the mark with distilled water. An aliquot of this solution was analyzed by either of the procedures.

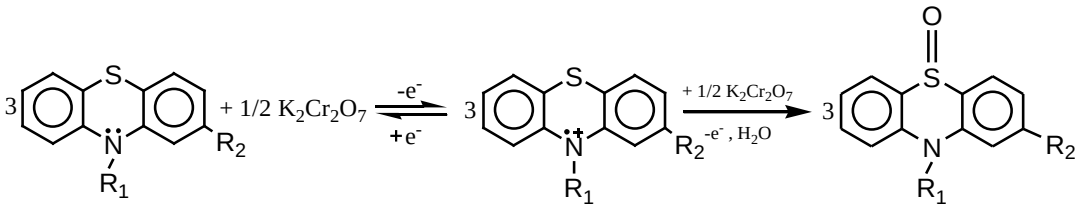
Injections:

The contents of twenty (Labeled to contain 25mg of phenothiazine) ampoules were mixed. After an a accurately measured volume equivalent to 20 ml of pure drug was transferred into a 100 ml standard flask and completed to the mark with distilled water, an aliquot was analyzed as was done for tables.

Results and Discussion:

Typical results of the proposed method are presented in tables(1) and (2). Table(1) represents the results of pure phenothiazines, whereas in table(2) the results of the phenothiazines in representative pharmaceutical formulations are compiled. These results are in good agreement with those obtained by the official British pharmacopoeia method.

The proposed method is based on the fact that potassium dichromate in an acid medium directly oxidizes Phenothiazine hydrochloride first to colored Phenothiazinium free radicals and finally to colorless sulfoxide,[14,15] after that the intensity of potassium ion content of the potassium dichromate was measured against a reagent blank. The oxidation of Phenothiazine drug is generally represented by scheme (1).



(Colorless) phenothiazine | (Colored) Radical Cation | (Colorless) Sulfoxide

	R_1	R_2
CPH	$-(CH_2)_3-N(CH_3)_2$	-Cl
TFPH	$-(CH_2)_3-N$ piperazine $N-CH_3$	$-CF_3$

Scheme (1) Reaction Scheme of Phenothiazine drug

Effect of Sulphuric Acid Strength:

When various concentrations of sulphuric acid solution were added to fixed of the drug solutions, 10ml of 10mol.l^{-1} solution was found enough to full intensity and was considered to be optimum for concentration rang 1-10mg of phenothaizine drug.

conc.(mol.L^{-1}) of H_2SO_4	1	2	4	6	8	10	12	1 4

4 6 9 1 2 3
5 3 6
I n t e n s i t y (a

Effect of Temperature:

The results of the proposed method were studied at different temperatures. The results indicate that the intensity values remain constant. Therefore room temperature (25ºC) is selected in this method.

Temperature(C°)	15	25	35	45	55
Intensity	33	36	36	34	34

Effect of Oxidant Concentration:

It was found that a 0.003mol.l^{-1} solution of potassium dichromate was recommended for all measurements.

The number of moles of dichromate consumed per mole of the drug was 0.333, in conformity with the formation of sulphoxides[16].

Con.(mol-1.L^{-1}) $K_2Cr_2O_7$	0.0005	0.001	0.002	0.003	0.004	0.005
Intensity	32	36	40	45	39	31

Table (1): Analytical Data

Parameter	CPH	TFPH
Beer's Law Limits (mg)	1-10	1-9
Recovery[a]	98.42	98.02
Regression Coefficient (r)	0.9981	0.9940
Slop (b)	9.1278	10.049
Intercept (a)	0.0602	1.4262

[a] **Average of six determinations each containing 10mg of drug.**

Interference:

Interference from the common additives and excipients likely to be present with the phenothaizine hydrochloride in formulations was investigated. Starch, Talc, Dextrose, Gelatin, Strearate and Alginate at the levels found in formulations did not interfere under the described experimental conditions, as shown by the results of the recovery study compiled in table (2).

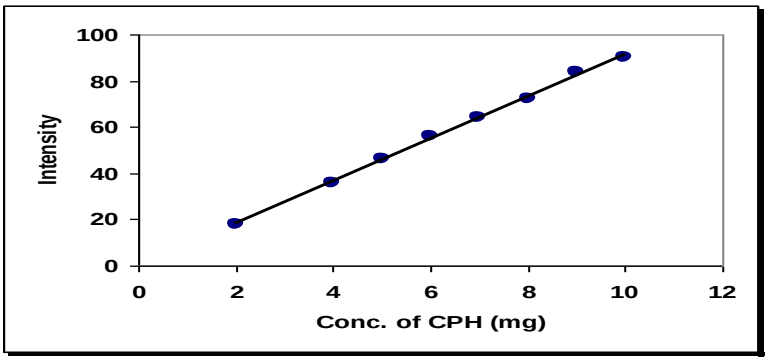
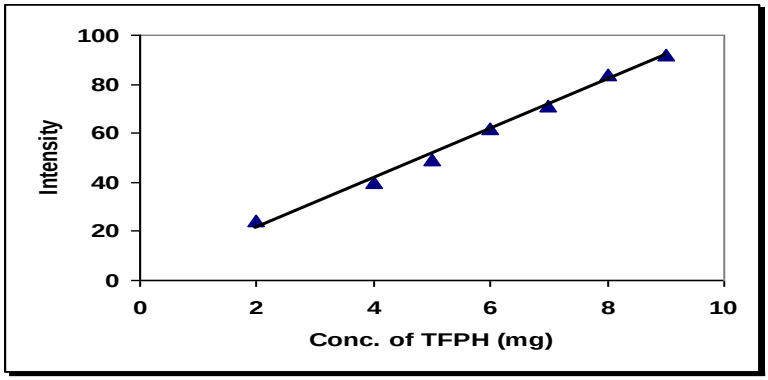


Fig. (1a): Calibration graph of Chloropromazine Hydrochloride



Fig(1b): Calibration graph of Trifluroperazine Dihydrochloride

The proposed method was applied to the determination of studied drug in their dosage forms. The results in table (2) indicate that the method give good accuracy and precision with satisfactory agreement with the results obtained by the official method.

Table (2): Assay of phenothiazines in pharmaceutical preparation by proposed method and reference methods

Formulation	Proposed Methods				Reference Method		
Taken	Found	Rec.%	S.D	Foun	Rec.	S.D	

Taken (mg)	(mg)			d (mg)	%		Tra zine [a]
Megatil[b] Tab.	25	24.60	98.4	0.60	25.42	101.7	0.50
Megatil Inj.	25	24.80	99.2	0.35	25.30	101.2	0.42

Data are presented as average of five determinations.
[a]Marketed by sun pharm Ltd.
[b]marketed by Intas.

The proposed methods were applied to the determination of studied drugs in their dosage forms. The results indicate that the methods give good accuracy and precision, with satisfactory agreement with the results obtained by the official method.

Conclusion:

Although phenothiazines have been determined by a variety of techniques, the method described here are simple, highly sensitive, convenient and don't require special working conditions, unlike many other reagents. Moreover, owing to the stability of the solid reagent as well as aqueous solution, dichromate can be used for routine analysis.

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