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Research Article

Indirect Spectrophotometric Quantification of Thioproperazine via Sulfoxide Formation

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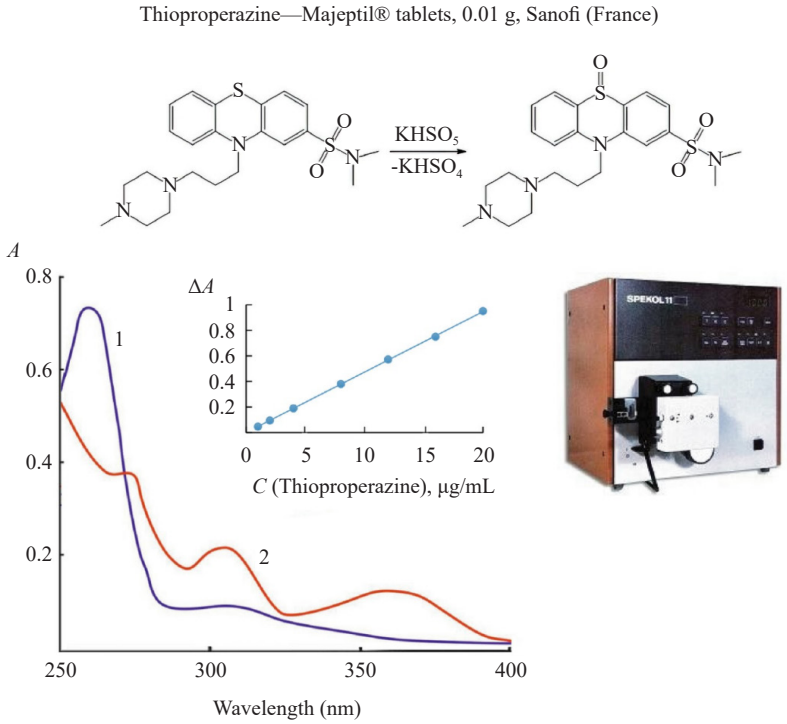

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Abstract: An indirect spectrophotometric approach was developed for the determination of Thioproperazine (TPZ) dimesylate in pharmaceutical dosage forms. The method is based on the oxidation of the drug with potassium peroxymonosulfate (potassium caroate), resulting in the formation of a sulfoxide derivative exhibiting a molar absorption coefficient $\varepsilon = 4.95 \times 10^3$ L·mol^{-1}·cm^{-1}. Quantification was achieved by measuring the absorbance at 353 nm using a corresponding non-oxidized TPZ solution of equal concentration as the reference. The absorbance difference (ΔA) followed Beer's law and showed linearity over the concentration range of 1-20 μg/mL, with the calibration equation $A = (47.3 \pm 0.3) \times 10^{-3} \times C$, where C is expressed in μg/mL. The limit of quantification was 0.6 μg/mL. The proposed method was successfully applied to the quantitative analysis of TPZ in Majeptil® tablets, which are labeled to contain 10 mg of active substance. The assay exhibited high selectivity, as common excipients and degradation products did not affect the analytical signal. The method demonstrated good precision (Relative Standard Deviation (RSD) = 1.3%) and accuracy, with a relative bias of + 0.5% compared to the reference pharmacopoeial method.

***Keywords*:** difference spectrophotometry, thioproperazine dimesylate, potassium peroxymonosulfate (caroate), sulfoxide formation, pharmaceutical analysis

1. Introduction

Thioproperazine, sold commercially as Majeptil®, is a conventional antipsychotic medication employed for its tranquilizing, antiemetic, and sedative properties, as well as in managing schizophrenia and manic episodes of bipolar disorder. It is formulated in 10 mg tablets.[1]

Thioproperazine is a piperazine derivative of phenothiazine. Structurally, it differs from prochlorperazine (chlorine substituent at position 2) and trifluoperazine (trifluoromethyl group at position 2) by the presence of a dimethylsulfamide group at the same position of the phenothiazine ring.[2] In pharmaceutical preparations, it is used as Thioproperazine (TPZ) dimesylate, chemically N,N-dimethyl-10-[3-(4-methylpiperazin-1-yl)propyl]phenothiazine-2-sulfonamide bis(methanesulfonate) (Figure 1).

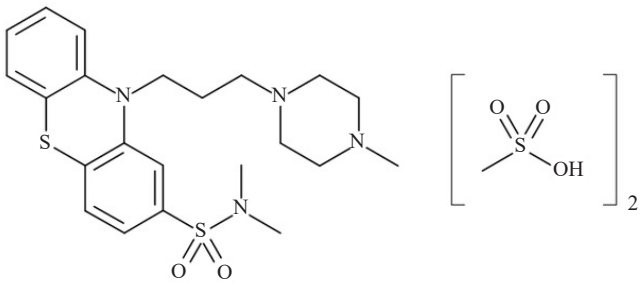

Figure 1. Structural formula of thioproperazine dimesylate

Phenothiazine derivatives remain an important subject of analytical and pharmaceutical research due to their extensive therapeutic applications. Existing analytical approaches for phenothiazines include chromatographic and spectrophotometric methods.

Official procedures rely on non-aqueous titration (United States Pharmacopeia (USP))[3] or Ultraviolet (UV)-visible spectrophotometry.[4] Quantitative methods for thioproperazine in plasma and urine have been reported, including solid-phase extraction followed by High Performance Liquid Chromatography (HPLC),[5] Liquid Chromatography-Mass Spectrometry (LC-MS),[6] HPLC-UV,[7] and fluorimetric methods.[8] Although highly sensitive, LC-MS techniques are costly and require specialized instrumentation.

An uncomplicated and sensitive spectrophotometric procedure for the quantitative measurement of thioproperazine mesylate has been described. The method is based on the formation of a phenothiazine radical cation upon oxidation

with N-bromophthalimide in a strongly acidic medium (methanol/sulfuric acid, 1 : 1 v/v). The resulting colored species exhibits a maximum absorbance at 516 nm. A linear relationship between absorbance at λ_{max} and drug concentration is observed in the range of 5-30 μg·mL^{-1}, with an apparent molar absorption coefficient ε of 9 × 10^3 L·mol^{-1}·cm^{-1}. Full color development requires approximately 25 minutes. The analytical results obtained with this method show good agreement with the official procedures of the British Pharmacopoeia (BP) and the United States Pharmacopeia (USP).[9] Nevertheless, it is well established that the stability of the radical-cation chromophore depends primarily on the oxidizing agent employed. When a strong oxidant is used, the radical color rapidly fades due to a secondary reaction step that converts it into a colorless sulfoxide. This process can significantly reduce both the sensitivity and the reproducibility of the analysis.

In general, this method has several disadvantages, including the requirement for a highly acidic medium, the use of toxic methanol, and the relatively long reaction time.[10]

As an alternative approach, a fast analytical method has been reported for the determination of phenothiazine-based drugs in various pharmaceutical dosage forms. This strategy employs difference spectrophotometry by comparing the absorbance of sulfoxide derivatives with that of the corresponding non-oxidized compounds. The sulfoxide products are generated rapidly and quantitatively at ambient temperature through oxidation with peracetic acid, which is produced in situ by the slow reaction of hydrogen peroxide with glacial acetic acid. The resulting absorbance difference between oxidized and untreated solutions correlates directly with the concentration of the phenothiazine derivative and provides selectivity toward the intact drug, even in the presence of excipients, colorants, flavoring agents, as well as oxidative and photochemical degradation products.[11] However, this approach requires a freshly prepared reagent solution due to its limited stability and the presence of a strong, irritating odor. To date, a simple, rapid, and selective spectrophotometric method for the analysis of thioproperazine that uses a stable oxidant compatible with green chemistry principles has not been described.

Accordingly, the aim of this work was to develop a simple and selective spectrophotometric procedure for the determination of thioproperazine in tablet formulations based on the formation of sulfoxide using a commercially available stable, environmentally friendly reagent—potassium peroxymonosulfate (potassium caroate).

This approach to performing the analysis of other phentazine derivatives has been previously implemented and has shown advantages over known methods.[12]

2. Materials and methods

2.1 *Chemicals*

Individual Thioproperazine dimesylate was obtained from Dayang Chem (Hangzhou) Co., Ltd. CAS Number: 2347-80-0. Chemical formula: $C_{22}H_{30}N_4O_2S_2/2CH_4O_3S$. Molecular weight 638.84100 g·mol^{-1}. Melting point: 218-222 °C.

Thioproperazine—Majeptil® tablets, 0.01 g, No. 20; Sanofi (France), batch 241062. Composition: Each film-coated tablet contains the following.

Active ingredient: thioproperazine dimesylate, 14.30 mg (equivalent to 10.00 mg thioproperazine free base). Other ingredients: lactose, wheat starch, colloidal hydrated silica, gelatin, sodium gentisate, ascorbic acid, magnesium stearate. Coating components: zein, butylacetoricinoleate.

2.2 *Equipment*

UV spectra of the oxidation products of TPZ and subsequent absorbance measurements were obtained using an Evolution 60S UV-visible spectrophotometer (Thermo Scientific, USA) with 1 cm quartz cells. For measurements requiring enhanced sensitivity, a Spekol 11 spectrophotometer (Carl Zeiss Jena) fitted with the EK-5 accessory and 50 mm pathlength cuvettes was employed.

2.3 *Design of experiments*

Preparation of a 0.02 mol/L $KHSO_5$ solution. Approximately 0.7 g of Oxone® ($2KHSO_5·KHSO_4·K_2SO_4$; Acros Organics) was dissolved in 70 mL of double-distilled water in a 100 mL volumetric flask, brought to volume at 20 °C,

and mixed thoroughly. The actual concentration of potassium peroxymonosulfate was verified by iodometric titration. For this purpose, 10 mL of the prepared solution was diluted to 100 mL, and a 10.00 mL aliquot of this diluted solution was transferred to an Erlenmeyer flask. After adding 1 mL of 0.01 mol/L H_2SO_4 and 2 mL of a 5% KI solution with continuous stirring, the liberated iodine was titrated immediately with 0.01 mol/L sodium thiosulfate. The molar concentration of $KHSO_5$ was calculated from three replicated titrations using the expression:

$$c(KHSO_5) = V(Na_2S_2O_3) \times 0.0100 \times 100.00/10.00 \times 10.00 \times 2.$$

Preparation of a solution of potassium hydrogen peroxomonosulfate 0.005 mol/L. A portion of about 0.15-0.2 g of Oxone ($2KHSO_5$, $KHSO_4$, K_2SO_4) was dissolved in 100 ml of double-distilled water. The exact content of potassium caroate was determined by iodometric titration.

2.4 *Identification of the S-oxidation product*

By the method of iodometric titration, it was established that in an acidic medium under conditions of excess oxidant, the reaction proceeds quantitatively and stoichiometrically (1 mol of $KHSO_5$ is consumed per 1 mol of TPZ) almost instantly with the formation of the corresponding sulfoxide of TPZ.

No further oxidation of the sulfoxide to the sulfone was observed within 30 minutes.

The recorded UV absorption spectrum of the Thioproperazine sulfoxide (TPZO) displays several distinct maxima, reflecting its characteristic electronic transitions. Prominent absorption peaks are observed at wavelengths of 218, 246, 274, 304, and 353 nm, each corresponding to specific features of the sulfoxide chromophore within the molecule. The molar absorption coefficients of these characteristic bands in 0.05 M H_2SO_4 were determined as follows (ε, $L \cdot mol^{-1} \cdot cm^{-1}$ at λ_{max}, nm): 2.20×10^4 (218 nm), 2.60×10^4 (246 nm), 1.50×10^4 (274 nm), 7.80×10^3 (304 nm), 4.95×10^3 (353 nm). These values agreed, within experimental error, with those reported in the literature.[13,14]

Additionally, the S-oxidation product of thioproperazine was characterized using fluorescence excitation and emission spectroscopy. The excitation and emission spectra were recorded at room temperature on an MPF-4 fluorescence spectrophotometer (Hitachi). The wavelengths of the characteristic excitation and emission maxima for the thioproperazine sulfoxide are presented in Table 1.

Table 1. Positions of excitation and emission maxima in the fluorescence spectra of thioproperazine sulfoxide (in 0.05 mol/L H_2SO_4)

Wavelength of maximum excitation (nm)				Wavelength of maximum emission (nm)		
233	272	304	345	360	465	504

3. Results

The present investigation demonstrated that TPZ can be efficiently quantified using a difference spectrophotometric technique that compares the absorbance of the sulfoxide product with that of the unoxidized compound. Upon addition of potassium peroxymonosulfate, introduced as the commercially available Oxone® reagent, a stable triple salt of composition $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, the corresponding sulfoxide was generated rapidly and quantitatively at ambient temperature. Compared with potassium peroxymonosulfate in its isolated form, Oxone® exhibits superior storage stability and an extended shelf life.[15] It is a white, readily water-soluble material that retains more than 99% of its oxidizing capacity after one month. The oxidizing strength of potassium peroxymonosulfate, characterized by a standard electrode potential of + 1.81 V for the hydrogensulfate-forming half-reaction under acidic conditions (pH = 0), underpins its effectiveness in this application.[16]

The difference in absorbance observed between the oxidized and corresponding non-oxidized solutions exhibits a direct proportional relationship with the concentration of the phenothiazine derivative present in the formulation. This

analytical signal is highly selective for the intact drug and remains unaffected by the presence of common excipients, colorants, flavoring agents, as well as oxidative or photochemical degradation products and most other substances typically encountered in pharmaceutical preparations.

The UV absorption spectra of thioproperazine mesylate (1) and thioproperazine sulfoxide (2) in 0.05 mol/L H_2SO_4 over the range of 250-375 nm are shown in Figure 2.

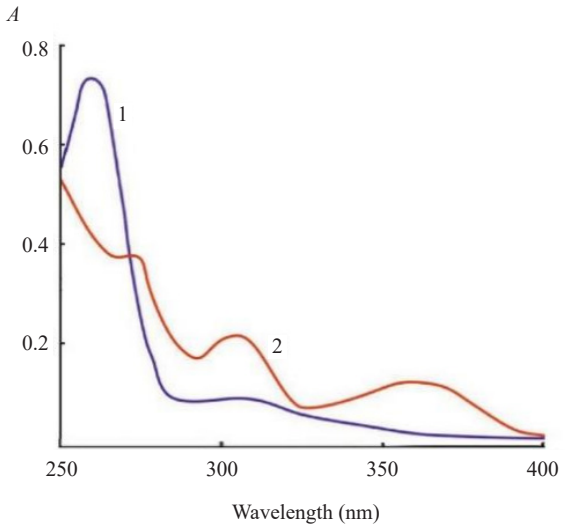

Figure 2. UV absorption spectra of thioproperazine (1) and thioproperazine sulfoxide, TPZO (2), in 0.05 mol/L H_2SO_4 within the range of 250-375 nm. Concentrations: c(TPZ) = 3.0×10^{-5} mol/L; c(TPZO) = 3.0×10^{-5} mol/L

Potassium caroate is a mild oxidizing agent, yet it readily converts TPZ to its sulfoxide (TPZO), as illustrated in Figure 3. As shown in Figure 2, TPZO exhibits a pronounced absorbance band at 353 nm, whereas TPZ itself shows only minimal absorbance at this wavelength. Therefore, 353 nm was selected for monitoring the formation of the oxidation product, with the residual absorbance of TPZ taken into account.

The molar absorptivity of thioproperazine sulfoxide was evaluated at its principal absorption maximum of 353 nm in 0.05 mol/L H_2SO_4. This parameter was obtained from the slope of the linear relationship between absorbance and concentration and was determined to be 4.95×10^3 L·mol^{-1}·cm^{-1}, reflecting the characteristic absorptive properties of the sulfoxide species under the selected experimental conditions.

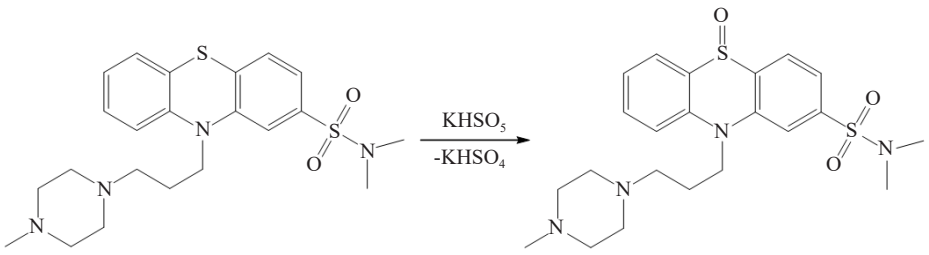

Figure 3. Scheme of thioproperazine oxidation by potassium caroate

3.1 *Procedure for constructing the calibration curve*

Preparation of the Working Standard Solution (WSS) of thioproperazine, 10.0 mg per 100 mL (as free base). A

portion of thioproperazine dimesylate (w = 98.44% active substance), accurately weighed at 0.01453 g, was transferred into a 100 mL volumetric flask. Approximately 70 mL of 0.05 mol/L H_2SO_4 was added, and the mixture was shaken for 10 minutes. The solution was then brought to volume with 0.05 mol/L H_2SO_4 at 20 °C and thoroughly mixed.

(A) Aliquots of 1.00, 2.00, 3.00, 4.00, 5.00, 10.00, and 15.00 mL of the WSS were transferred into 25 mL volumetric flasks. To each flask, 2.5 mL of 0.5 mol/L H_2SO_4 and 1.5 mL of 2 mmol/L $KHSO_5$ were added, and the solutions were diluted to volume with distilled water. The absorbance was measured at 353 nm using a 1.2×10^{-4} mol/L $KHSO_5$ solution as the reagent blank. These data were used to determine the molar absorptivity (ε).

(B) Aliquots of 1.00, 2.00, 3.00, 4.00, 5.00, 10.00, and 15.00 mL of the working standard solution were transferred into 25 mL volumetric flasks. To each flask, 2.5 mL of 0.5 mol/L H_2SO_4 and 1.5 mL of 2 mmol/L $KHSO_5$ were added, and the solutions were diluted to volume with distilled water. The absorbance was measured at 353 nm using, as the compensating solution, the corresponding non-oxidized preparation prepared in the same manner but without the addition of $KHSO_5$.

The calibration curve for the quantitative determination of thioproperazine mesylate (expressed as the free base) in the form of its sulfoxide by difference spectrophotometry—relative to the non-oxidized thioproperazine solution, in 0.05 mol/L H_2SO_4, using a 50 mm pathlength cuvette at λ = 353 nm—is shown in Figure 4. The linear regression equation obtained was: $A = (47.3 \pm 0.3) \times 10^{-3} \times C$, where C is the concentration in µg/mL. The Limit of Quantification (LOQ) was 0.6 µg/mL (Table 2).

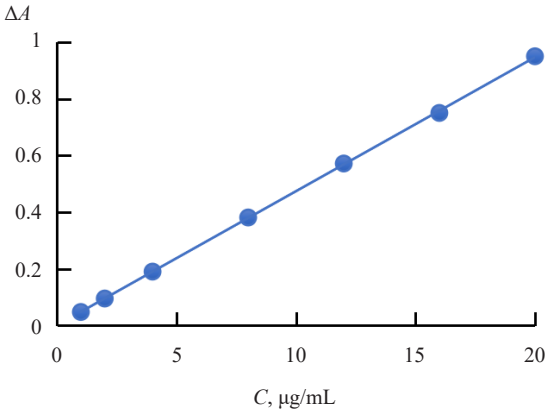

Figure 4. Calibration curve for the quantitative determination of thioproperazine mesylate (expressed as the free base) in the form of its sulfoxide by difference spectrophotometry (relative to the non-oxidized thioproperazine solution). Conditions: 0.05 mol/L H_2SO_4; cuvette pathlength 5 cm; λ = 353 nm

Table 2. Analytical characteristics of the calibration graph ($y = a + bx$) for the quantification of thioproperazine mesylate in the form of its sulfoxide by difference spectrophotometry

Characteristics	Parameters
Concentration range (µg·mL^{-1})	1-20
Linear regression equation	$y = 0.0473x + 0.001$
Correlation coefficient (r)	0.9998
Slope ($b \pm \Delta b$)	0.0473 ± 0.0003
Intercept ($a \pm \Delta a$)	0.001 ± 0.0003
Standard Deviation (S.D.) of slope (Sb)	0.0003
Standard Deviation (S.D.) of intercept (Sa)	0.0003
Limit of Detection (LOD) (3S) (µg·mL^{-1})	0.19
LOQ (10S) (µg·mL^{-1})	0.6

3.2 *Accuracy and precision*

Repeatability was calculated as the relative standard deviation (multiplied by 100 to obtain % value) of five consecutive measurements. For determination of repeatability, TPZ standards of 4.0, 8.0, and 12.0 µg/mL concentration were used. Recovery was determined from analysis of 4.0, 8.0, and 12.0 µg/mL TPZ standard solutions and was calculated as the ratio of measured and real concentration multiplied by 100 to achieve a value in %. The results of the quantitative determination of thioproperazine mesylate (based on the base) in pure solutions are shown in Table 3.

Table 3. Evaluation of precision and accuracy (n = 5; P = 0.95)

Amount taken (μ), µg/mL	Amount found, µg/mL	Recovery ± RSD, %	δ*, %
4.00	4.01 ± 0.11	100.25 ± 2.2	+ 0.25
8.00	8.03 ± 0.16	100.375 ± 1.6	+ 0.375
12.00	12.05 ± 0.18	100.42 ± 1.2	+ 0.40

Note: * Systematic error (δ) calculated by $(\bar{x} - \mu) \times 100/\mu$ (%)

3.3 *Practical application in pharmaceutical analysis*

3.3.1 *Analysis procedure*

Procedure for the quantitative determination of thioproperazine in Majeptil® 10 mg tablets using the standard method. A portion of the powdered, triturated tablets corresponding to the average tablet mass was transferred into a 100 mL volumetric flask. Approximately 70 mL of 0.05 M H_2SO_4 was added, the mixture was shaken for 10 minutes and then filtered. The filtrate was diluted to volume with 0.05 M H_2SO_4.

An aliquot of 5.00 mL of this solution was transferred by pipette into a 25 mL volumetric flask, followed by the addition of 2.5 mL of 0.1 M H_2SO_4 and 1.5 mL of 2 mmol/L $KHSO_5$. The solution was then diluted to volume with distilled water. The absorbance at 353 nm was recorded using, as the compensating solution, a corresponding thioproperazine solution prepared as follows: a 5.00 mL aliquot of the tablet extract was placed into a 25 mL volumetric flask, 2.5 mL of 0.1 mol/L H_2SO_4 was added, and the solution was diluted to volume with distilled water (without $KHSO_5$).

The analysis was performed in the same manner using the WSS of thioproperazine at a concentration of 10.0 mg per 100 mL. The absorbance at 353 nm was measured using the corresponding non-oxidized standard solution prepared analogously but without the addition of $KHSO_5$.

The content of thioproperazine free base ($C_{22}H_{30}N_4O_2S_2$) in the tablets, expressed as a percentage of the labeled amount (X), is calculated using the following equation:

$$X = \frac{\Delta A_1 \times a_0 \times P \times G}{\Delta A_0 \times a_1 \times L},$$

where:

ΔA_1: absorbance measured for the test (tablet) solution;

ΔA_0: absorbance measured for the WSS thioproperazine standard solution;

a_1: mass of the powdered, triturated tablets taken for analysis (mg);

a_0: mass of the thioproperazine standard substance taken (mg);

P: content of active substance in the thioproperazine standard (%);

G: average mass of one tablet (mg);

L: labeled content of thioproperazine free base ($C_{22}H_{30}N_4O_2S_2$) in one tablet (mg).

3.3.2 *Specificity*

To assess method specificity, various substances that could be present in the dosage form, either as formulation excipients or as degradation products, were tested under the proposed assay conditions for their effect on the absorbance difference measured at 353 nm. None of the examined compounds produced a detectable absorbance signal at this wavelength. Specifically, thioproperazine sulfoxide and, within pharmaceutically acceptable concentration ranges, lactose, wheat starch, colloidal hydrated silica, gelatin, sodium gentisate, ascorbic acid, magnesium stearate, casein, and butylacetoricinoleate did not interfere with the determination. To assess possible interference, varying amounts of substances that may be introduced during the manufacturing process were added to a constant amount of thioproperazine mesylate (14.3 mg, corresponding to 10 mg of the free base), after which the proposed spectrophotometric procedure was carried out (Table 4).

Table 4. Tolerable amounts of potential interfering excipients or degradation products that do not cause an absorbance change greater than + 0.005 at 353 nm (relative to 10 mg thioproperazine mesylate, expressed as free base)

Potential interferents, including inactive formulation components and oxidative or photochemical degradation products	The amount without interfering[a] (mg)
Excipients:	
Cellulose microcrystalline	50
Lactose monohydrate	100
Wheat starch	12
Magnesium stearate	3
Gelatin	3
Sodium gentisate	9
Colloidal silicon dioxide	1.8
Ascorbic acid	2
Oxidative and photochemical decomposition products:	
Thioproperazine sulfoxide	2
Coating excipients:	
Zein	20
Butylacetoricinoleate	10.8
Sucrose	55
Calcium carbonate	10.8
Povidone K25	0.6
Yellow quinoline	0.006
Indigo carmine	0.006
Macrogol 35000	0.85
Titanium dioxide	0.8
Carmellose sodium	0.6
Polysorbate 20	0.6

[a] The value represents the mass of each excipient, relative to 10 mg of thioproperazine mesylate (expressed as the free base), that does not produce an absorbance change greater than + 0.005

The indirect UV-spectrophotometric method for determining thioproperazine in the form of its sulfoxide proved to be reliable. The developed quantitative procedure enables the determination of thioproperazine over the concentration interval of 1-20 μg/mL. The LOQ (10S) is 0.6 μg/mL. The results obtained were unaffected by the presence of excipients or degradation products in the dosage form. The precision of the method was RSD = 1.3%, and the relative bias $(\bar{x} - \mu) \times 100\%/\mu = + 0.5\%$, where μ represents the quantitative value obtained by the reference pharmacopoeial method as stated in the certificate of analysis (Table 5). The fulfillment of the inequality $|(\bar{x} - \mu) \times 100\%/\mu| < t_{\alpha} \times \text{RSD}/\sqrt{n}$ confirms the absence of systematic error, indicating that the analytical results are accurate.

Table 5. Assay results for Majeptil® tablets containing 10 mg thioproperazine using the developed spectrophotometric method ($n = 5$; $P = 0.95$)

Analyte/product tested	Found ($\bar{x} \pm \Delta x$), mg/tablet (Recovery, %)	RSD, %	Certificate value (μ*), mg/tablet	$\frac{(\bar{x} - \mu)}{\mu *}100$, %
Thioproperazine, Majeptil® tablets 0.01 g, No. 20; Sanofi (France), batch 241062	10.05 ± 0.16 (100.5 ± 1.60%)	1.30	10.00	+ 0.5

* Data obtained using the official HPLC method as reported in the certificate of analysis

4. Conclusions

The results of this study demonstrate that potassium peroxymonosulfate (caroate) can be used as an efficient, selective, and analytically robust oxidizing agent for converting Thioproperazine (TPZ) to its sulfoxide (TPZO), which exhibits a well-defined absorption maximum at 353 nm. This wavelength allows reliable difference spectrophotometric measurement due to the minimal absorbance of the parent compound, thus ensuring high selectivity of the proposed approach.

The rapid and quantitative formation of TPZO at room temperature represents a significant analytical advantage compared with previously reported methods based on cation-radical formation using N-bromophthalimide. Such older procedures require highly acidic media, extended reaction times, and suffer from instability of the radical chromophore, which leads to over-oxidation and diminished reproducibility. In contrast, the oxidation with potassium caroate proceeds smoothly, avoids strongly corrosive conditions, and yields a stable sulfoxide product, aligning the method more closely with principles of green chemistry.

The linearity of the calibration graph over a wide concentration range (1-20 μg/mL) and the excellent correlation coefficient confirm that Beer's law is obeyed under the experimental conditions. The achieved the molar absorption coefficient ($\varepsilon = 4.95 \times 10^3$ L·mol^{-1}·cm^{-1}) is consistent with literature values for phenothiazine sulfoxides, further validating the identification of the oxidation product. The low limit of quantification (0.6 μg/mL) highlights the sensitivity of the method and makes it suitable for routine quality control as well as potential use in stability studies.

A key strength of the method is its specificity. Common tablet excipients, as well as oxidative and photolytic degradation products, did not interfere with pharmaceutically relevant concentrations. This indicates that the absorbance difference (ΔA) is uniquely attributable to the intact thioproperazine molecule and not to its undesirable transformation products. Such specificity is particularly important for drugs of the phenothiazine class, where structural analogues and degradation pathways often complicate spectrophotometric analyses.

Application of the method to Majeptil® tablets showed high accuracy and precision. The experimentally determined content (10.05 mg per tablet) was in excellent agreement with the certified value (10.00 mg), giving a relative bias of only + 0.5%. The RSD of 1.3% confirms good method repeatability. Statistical evaluation demonstrated that no systematic error was present, supporting the reliability and reproducibility of the proposed procedure.

Overall, the data indicate that the indirect spectrophotometric determination of thioproperazine via its sulfoxide is not only analytically sound but also operationally simple and environmentally favorable. Compared to existing spectrophotometric or chromatographic techniques, the method requires no hazardous reagents, no specialized equipment, and minimal sample preparation. These advantages make it particularly suited for routine laboratory use, including settings where advanced chromatographic instrumentation may not be available.

5. Limitations and future perspectives

Since the main disadvantage of direct UV spectrophotometry is its pronounced sensitivity to excipients commonly present in pharmaceutical preparations, analytical methods based on controlled oxidation reactions may represent a valuable alternative. In particular, the absorption of the S-oxide of phenothiazine derivatives is significantly less susceptible to spectral interference from other pharmaceutical ingredients. This characteristic makes oxidation-based spectrophotometric approaches suitable for the determination of these drugs in the presence of degradation products formed during oxidative stress or storage.

The statistical evaluation and recovery studies performed in this work confirm the accuracy and reproducibility of the proposed method. In addition to its adequate sensitivity, the procedure benefits from operational simplicity and the low cost of both instrumentation and reagents. The method also demonstrates a high tolerance toward excipients typically encountered in pharmaceutical formulations, further supporting its reliability in routine analysis.

Taken together, these features suggest that the proposed indirect spectrophotometric method is well-suited for application in routine quality control laboratories, particularly where rapid analysis, cost efficiency, and high selectivity are required. Future investigations may extend this approach to other phenothiazine derivatives and dosage forms, as well as explore its potential utility in stability studies and comparative assessments with more instrument-intensive analytical techniques.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

[1] Brayfield, A.; Cadart, C. *Martindale: The Complete Drug Reference*, 41st ed.; Pharmaceutical Press: London, 2024.

[2] Turkewich, M. M.; Vladzimirska, O.; Lesyk, R. *Pharmaceutical Chemistry (Steroid Hormones, Their Synthetic Analogues and Heterocyclic Compounds as Medicinal Agents)*; Nova Knyha: Lviv, 2003.

[3] United States Pharmacopeial Convention. *The United States Pharmacopeia*, 27th ed.; United States Pharmacopeial Convention: Rockville, MD, 2004.

[4] British Pharmacopoeia Commission. *The British Pharmacopoeia*; HMSO: London, 2001.

[5] Marumo, A.; Kumazawa, T.; Lee, X.-P.; Fujimaki, K.; Kuriki, A.; Hasegawa, C.; Sato, K.; Seno, H.; Suzuki, O. Analysis of phenothiazines in human body fluids using disk solid-phase extraction and liquid chromatography. *J. AOAC Int*. **2005,** *88*(6), 1655-1660.

[6] Rodrigo Valero, A. M.; Quintela Jorge, O.; Bravo Serrano, B.; Ayuso Tejedor, S. Optimization of a rapid method for screening drugs in blood by liquid chromatography tandem mass spectrometry. *Adv. Lab. Med*. **2023,** *4*(4), 365-371.

[7] Tanaka, E.; Nakamura, T.; Terada, M.; Shinozuka, T.; Hashimoto, C.; Kurihara, K.; Honda, K. Simple and simultaneous determination for 12 phenothiazines in human serum by reversed-phase high-performance liquid chromatography. *J. Chromatogr. B* **2007,** *854*(1-2), 116-120.

[8] Laassis, B.; Maafi, M.; Aaron, J.-J.; Mahederob, M. Fluorimetric and photochemically induced fluorimetric determination of ethopropazine, levomepromazine, thioproperazine, and trifluoperazine. *Anal. Lett*. **1997,** *30*(8), 1541-1554.

[9] El-Kerdawy, M. M.; Hassan, S. M.; El-Ashry, S. M. Spectrophotometeric determination of some N-substituted phenothiazine derivatives using N-bromophthalimide. *Mikrochim. Acta* **1992,** *108*, 323-328.

[10] Puzanowska-Tarasiewicz, H.; Kuźmicka, L.; Karpińska, J.; Mielech-Łukasiewicz, K. Efficient oxidizing agents for determination of 2,10-disubstituted phenothiazines. *Anal. Sci*. **2005,** *21*, 1149-1153.

[11] Davidson, A. G. The determination of phenothiazine drugs in pharmaceutical preparations by a difference spectrophotometric method. *J. Pharm. Pharmacol*. **1976,** *28*(11), 795-800.

[12] Blazheyevskyi, M. *Application of Derivatization by Means of Peroxyacid Oxidation and Perhydrolysis Reactions in Pharmaceutical Analysis*; Ivan Franko National University of Lviv: Lviv, 2017.

[13] De Leenheer, A. Ultraviolet spectrophotometry of phenothiazine derivatives and analogs. *J. Assoc. Off. Anal.*

Chem. **1973,** *56*(1), 105-118.
[14] Fujisawa, M.; Kawabata, A. Pharmaceutical studies on phenothiazine derivatives. V.: photolysis of thioproperazine, acetylpromazine, and their sulfoxides. *Yakugaku Zasshi* **1966,** *86*(6), 510-514.
[15] Crandall, J. K.; Shi, Y.; Burke, C. P.; Buckley, B. R. Potassium monoperoxysulfate. In *Encyclopedia of Reagents for Organic Synthesis*; John Wiley & Sons: Chichester, 2001.
[16] Spiro, M. The standard potential of the peroxosulphate/sulphate couple. *Electrochim. Acta* **1979,** *24*(3), 313-314.