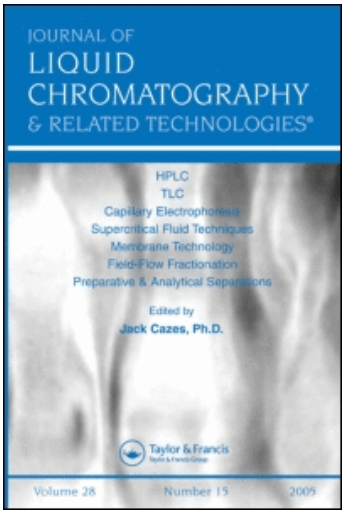

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Simultaneous Quantitation of Some Phenothiazine Drug Substances and Their Monosulphoxide Degrades by High Performance Liquid Chromatography(HPLC)

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SIMULTANEOUS QUANTITATION OF SOME PHENOTHIAZINE DRUG SUBSTANCES AND THEIR MONOSULPHOXIDE DEGRADES BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY(HPLC)

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ABSTRACT

A simple liquid chromatographic procedure is presented for the simultaneous quantitation of three phenothiazine drugs, namely, perphenazine, trifluoperazine and triflupromazine and their sulphoxide degrades. The LC-separation was performed on a Novapak-phenyl-4 (150 x 3.9 mm id) column and a mobile phase composed of methanol + 1.5 x 10^{-2} M sodium acetate buffer pH 6.5 (81:19, v/v). Isocratic elution and UV-detection were adopted. Satisfactory percent assay and mean recoveries with low relative standard deviations were obtained for each drug and its sulphoxide in bulk and in tablet dosage form.

The stability-indicating characteristics of the presented LC-procedure prove its advantage over the pharmacopeial methods used to limit the sulphoxides.

INTRODUCTION

The phenothiazine drugs are clinically used as tranquillizers for the treatment of moderate and servere mental and emotional disturbances.[1] Chemically, these drugs are unstable as they decompose under the effect of various factors such as light, heat, oxygen and metal ions, particularly when existing in solution. Official monographs direct that preparations of phenothiazine drugs be protected from exposure to light and air, and ampoules filled under nitrogen.

It is believed that under mild changes of conditions,[2,3] the decomposition oxidation products are mainly the monosulphoxides some of which are found to be significantly less potent than the parent compounds.[4] However, mesoridazine, which is a side-chain monosulphoxide metabolic product of thioridazine, is well known to be psychoactive.[5-8] More serious is chlorpromazine sulphoxide which is as active pharmacologically as the parent compound, but it is suspected of causing photo-toxic side effects associated with chronic use of chlorpromazine.[9,10,11] It is this reason that has investigated many workers to explore reliable methods for the simultaneous quantitation of phenothiazine drugs and their sulphoxide degrades in bulk form and in pharmaceutical formulations.

Several quantitative analytical procedures based on ordinary spectrophotometry[12-15] were reported for the determination of phenothiazine drugs and their sulphoxides. But the ordinary spectrophotometric method lacks sensitivity and selectivity. Furthermore, second derivative spectrofluorometry alone[16] or combined with TLC,[17] second derivative and third-derivative UV-spectrophotometry,[18] and GLC[19] were also proposed.

Although the derivative UV-spectrophotometric procedures are more selective than the ordinary ones, yet the sensitivity is not improved. On the other hand, GLC exhibits adequate sensitivity and selectivity, but the phenothiazine intact molecule breaks down readily under the relatively high temperature utilized in the analysis.

For the three phenothiazine drugs investigated in this work, namely, perphenazine (PR), trifluperazine (TF) and trifluopromazine (TP), the British Pharmacopoeia (BP)[20] and the United States Pharmacopeia (USP),[21] adopt titrimetry and ordinary spectrophotometry for the assay of the raw drug and their tablet formulations, respectively.

In the present work, a high performance liquid chromatography (HPLC) is elaborated for the simultaneous assay of each of PR, TP and TM and their sulphoxides. The work clearly indicates the superiority of HPLC in the accurate determination of trace amounts of sulphoxide impurities that may contaminate the parent phenothiazine drug.

EXPERIMENTAL

Materials

Reference perphenazine (Lot No. P-4320) and trifluoperazine (Lot No. T-4333) were purchased from Winlab (U.K.). Triflupromazine reference material was purchased from Sigma Chemical Co. (U.S.A.). The powder materials of the three phenothaizine drugs were used without further treatment.

Perphenazine tablet formulations (Trilafon®-4 mg, Lot No. 91 L 160413) and trifluoperazine hydrochloride (Apo-Trifluoperazine-5 mg tablets, BN S-8260), were obtained from Schering (U.S.A.) and Apotex (Canada), respectively, through their Medical Representative Offices in Riyadh, Saudi Arabia.

Trifluoperazine hydrochloride (Stelazine®-5 mg tablet, BN 5800 and Stelazine®-1 mg tablet, BN 3030) were the products of SK & K (U.K.) and were kindly received from King Khalid University Hospital, King Saud University, Riyadh.

Water employed was all-glass doubly distilled. Methanol and acetonitrile (BDH) and chloroform (Fluka) used in chromatographic investigations were HPLC grade.

For the preparation of different buffer systems, sodium acetate trihydrate (Merck-AnalaR), boric acid (BDH-AnalaR), 85% orthophosphoric acid (Merck) and citric acid (Hopkin & William-AnalaR), were utilized.

Dodecyl sodium sulphate which served as ion-pairing reagent in ion-pair chromatographic experiments and hydrogen peroxide (Perhydrol-30% H_2O_2)

used for the preparation of peroxyacetic acid needed for the oxidation of parent phenothiazine drugs to their respective monosulphoxides, were the products of Merck.

Apparatus

The liquid chromatograph employed for the preliminary chromatographic investigations was Varian Model 5000 equiped with single piston reciprocating pump, pulse damper and high pressure injector Rheodyne 7125 of 20 µL loop. Varian variable wavelength UV-Visible detector model UV 50, CDS 111L integrator and recorder model 9176 were attached.

After fine-tuning of method development, the system used consisted of Waters 600 E liquid chromatograph equiped with injector U6K and Waters 486 tunable absorbance detector.

The column utilized was chemically bonded Novapak-phenyl-4, 150 x 3.9 mm id (Waters) and the mobile phase consisted of methanol and 1.5 x 10^{-2} M sodium acetate buffer of pH 6.5 (81:19, v/v). The optimum flow rate of the mobile phase and the UV detection were determined for each compound.

Measurements and adjusments of pH for solutions were made using the pH-meter Model 523 WTW (Germany).

Reagents

Peroxyacetic acid (CH_3COOOH)

Prepared by diluting 5 mL 30% H_2O_2 to 500 mL of glacial acetic acid and allowing to stand overnight at room temperature. This reagent when added to parent phenothiazine drug in methanol yields quantitatively the respective monosulphoxide.

Standard solutions of reference phenothiazine drug substance (025% w/v)

For each of the three phenothiazine drugs 25 mg of reference material was accurately weighed, transferred into 100 mL calibrated flasks and dissolved in methanol. All the flasks should be wrapped with aluminium foil since the phenothiazine derivatives are prone to photodegradation.

Methods

Preparation of the phenothiazine drug monosulphoxide

Based on Davidson's procedure (3,12) 5 mL-volume of peroxyacetic acid was added to 5 mL of the reference phenothiazine drug solution. The reaction mixture was left to stand at room temperature for 15 min. The completeness of the reaction was checked by TLC using silica plates. To remove excess glacial acetic acid and alcohol, the reaction mixture was evaporated under *vacco* at room temperature using oil pump. The residue of the sulphoxide obtained was dissolved in the appropriate solvent to yield a standard solution of the sulphoxide required for further work.

Establishment Of calibration curves

Standard series

From the stock methanolic solution of perphenazine (25 μg mL^{-1}) 1, 2,..., 6 mL portions were transferred into six 25-mL volumetric flasks followed by 1, 2,..., 6 mL portions of the standard perphenazine-sulphoxide solution. The internal standard solution was added (final concentration 3 μg mL^{-1}) to each flask before completion to volume with the mobile phase. The standard ratios of peak-area responses for perphenazine and perphenazine sulphoxide to the internal standard using triplicate injections of 10 μL were calculated for each solution. The mean ratios were plotted versus concentration of the parent drug and the sulphoxide. Alternatively, linear regression equations could be worked out using the least squares method. The procedure was repeated for trifluoperazine and triflupromazine and their sulphoxides.

Sample preparations

Twenty perphenazine tablets (Trilafon®-4 mg) were accurately weighed and finely powdered. The mean mass of material per tablet was calculated and a portion of powder containing about 4 mg of the active ingredient was accurately weighed. About 5 mL of water was added and the mixture was heated for 3 min on a water-bath. After cooling, approximately 50 mL of water was added and the mixture was shaken for about 15 min before completion of volume to 100 mL with methanol. The mixture was filtered and 5 mL volume of the filtrate was transferred into a 50 mL calibration flask, followed by the internal standard and adjustment of volume with the mobile phase.

The procedure was exactly repeated for trifluoperazine and triflupromazine tablets.

Procedure

Triplicate volumes of 10 μL each of the standard and sample preparations of perphenazine were injected into the chromatograph. The mean peak-area response ratios (Y) of perphenazine to the internal standard for the standard and sample preparations were calculated. The amount of perphenazine per tablet was computed from the expression:

$$\text{Amount of perphenazine (mg / tablet)} = \frac{A_1}{A_2} \times C \times \frac{W_1}{W_2}$$

where A_1 is the peak-area ratio of the sample, A_2 is the peak-area ratio of the standard, W_2 is the mass of portion of powder taken and C is the concentration of the final diluted standard solution.

Similarly the contents per tablet for trifluoperazine and triflupromazine determined.

Analysis Of Binary Mixtures Of The Parent Phenothiazine Drug And Its Sulphoxide

To investigate the capability of the elaborated HPLC method for the simultaneous quantitation of perphenazine, trifluoperazine and triflupromazine in presence of their respective sulphoxides, a set of HPLC experiments were performed using synthetic mixtures of each phenothiazine and its sulphoxide and powdered tablet samples spiked with the appropriate standard sulphoxide solution.

The ratio (m/m) for the binary mixtures and spiked samples was varied in such a way that the percentage of sulphoxide to parent compound spanned the range from 25 down to 0.25%.

The BP method[20] of assay was applied to the same solution analysed by the elaborated HPLC method and the results obtained were compared (See conclusion).

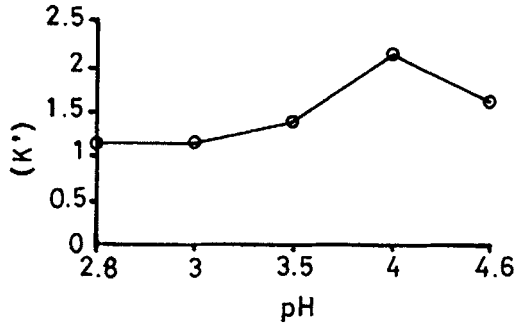

Figure 1: Capacity Factor (k') versus pH.

RESULTS AND DISCUSSION

The elaboration of an adequate liquid chromatographic method to address a given separation is usually performed by undertaking preliminary investigations involving various chromatographic systems. In this study of the three phenothiazine drugs and their sulphoxides, experiments were carried out using TLC, reverse phase ion-pair and reverse phase liquid chromatography. The results of the TLC on silica plates yielded acceptable R_f values (~0.5) for each drug and its sulphoxide employing a mobile phase consisting of methoanol and 1.5 x 10^{-2} M ammonium acetate buffer of pH 6.5 (75:25, v/v). This indicates that the methanol-acetate buffer system is potentially a suitable mobile phase.

Systematic investigations by adopting reverse phase liquid chromatography using μ-Bondapak C_{18}-10 (300 x 3.9 mm id) and Novapak phenyl-4 (150 x 3.9 mm id) columns with a mobile phase consiting of methanol, water, acetonitrile and 1.5x 10^{-2} M-sodium acetate buffer of pH 6.5, in varying proportions. Excellent separation was obtained on Novapak-4 column and methanol + 1.5 x 10^{-2} M-sodium acetate, pH 6.5 (81:19, v/v).

Similar studies for the suitability of reverse-phase ion-pair chromatography with μ-Bondapak C_{18}-10 (300 x 3.9 mm id) column, methanol + 1.50 x 10^{-2} M-sodium acetate mobile phase and sodium dodecyl sulphate as ion-pair forming reagent i.p.f.r. were conducted. Typical results of the effects of parameters such as pH and concentration of i.p.f.r. on capabcity factor (k') for perphenazine are demonstrated in Figs. 1 and 2.

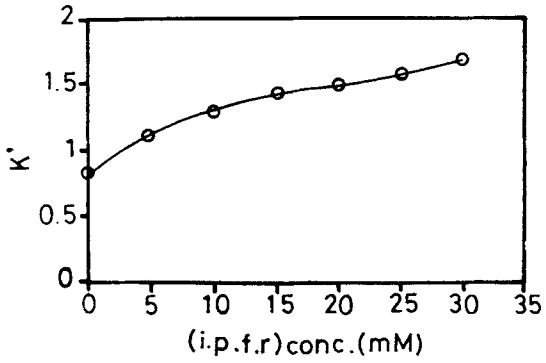

Figure 2: Capacity factor (k') versus concentration of ion pair forming reagent (i.p.f.r.).

As shown in Fig. 1, the increase in the pH of the mobile phase from 2.8 to 4.0 leads to an increase in the capacity factor (k') which decreases above pH 4.0. It was observed that at pH ≥ 6.5 the peak of perphenazine chromatogram was too broad leading to low sensitivity.

The effect of concentration of the i.p.f.r. was studied by adding varying amounts of sodium dodecyl sulphate to perphenazine in the mobile phase at pH 4.0. As a result of formation of an adduct of lower polarity than that of perphenazine alone, a better separation was expected. Figure 2 depicts typical findings for perphenazine where a steady increase of capacity factor, k', with the increase in the concentration of i.p.f.r. at pH 4.0 is observed.

The effect of buffer concentration on the chromatographic separation by ion-pair chromatography was investigated by utilizing increasing concentration of the acetate in the range 0.05 to 0.7 M at constant pH and ionic strength. A substantial reduction of the peak height occurred at buffer concentration above 0.1 M. This reduction might be due to the decreased formation of the ion-pair adduct owing to competition between dodeceyl sulphate and acetate ions.

Although separation parameters were worked out by adopting both reverse phase and ion-pair reverse phase chromatography, the former mode of liquid chromatography proved to be more satisfactory. Table 1 assembles the final chromatographic parameters worked out by employing HPLC in the reverse-phase mode. Figures 3-5 represent typical chromatograms for the three phenothiazine drugs studied, their respective sulphoxides and the internal standard.

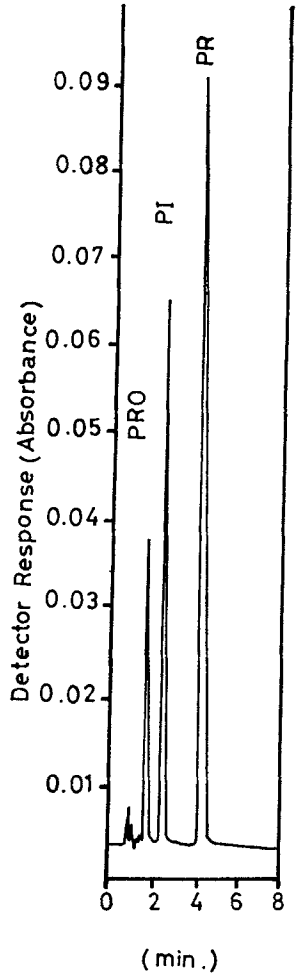

Figure 3: Chromatogram of perphenazine (PR), perphenazine sulphoxide (PRO) and pindolol (PI) as internal standard. AUFSD = 0.1, 10 μL injected. Retention times are 4.4, 1.7 and 2.5 minutes for PR, PRO and PI respectively. UV-detection at 254 nm, mobile phase flow rate 1.0 mL/min.

To test the suitability of the proposed HPLC system and to validate its performance characteristics such as precision, accuracy, linearity, limit of detection and ruggedness, a number of experiments were performed using the

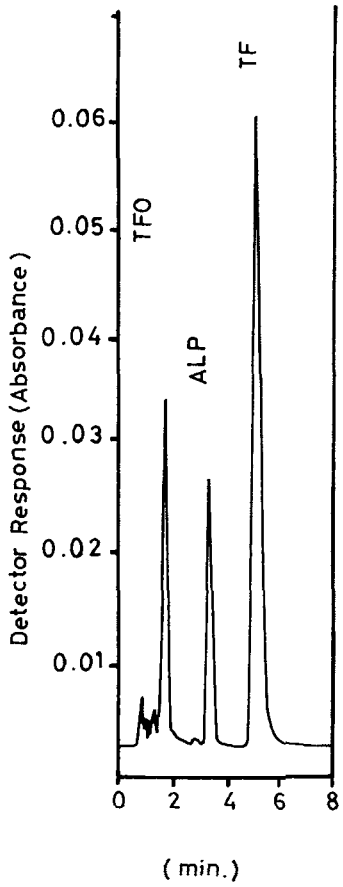

Figure 4: Chromatogram of trifluoperazine-2HCl (TF), trifluoperazine-sulphoxide (TFO) and alprenolol (ALP) as internal standard. AUFSD = 0.1, 10 μL injected. Retention times are 5.5, 1.8 and 3.4 minutes for TF, TFO and ALP respectively. UV-detection at 254 nm, mobile phase flow rate 1.2 mL/min.

three phenothiazine drugs (in bulk and in dosage form) and their sulphoxides. The entries of Tables 2 (a, b, c) summarize the ranges of concentrations employed and average peak-area response ratios (Y), for each phenothiazine drug and its sulphoxide. The intercept (A), the slope (B) and the correlation coefficient (r) of the best fit line was determined by least squares regression analysis. The detection limit (DL), which is the lowest detectable

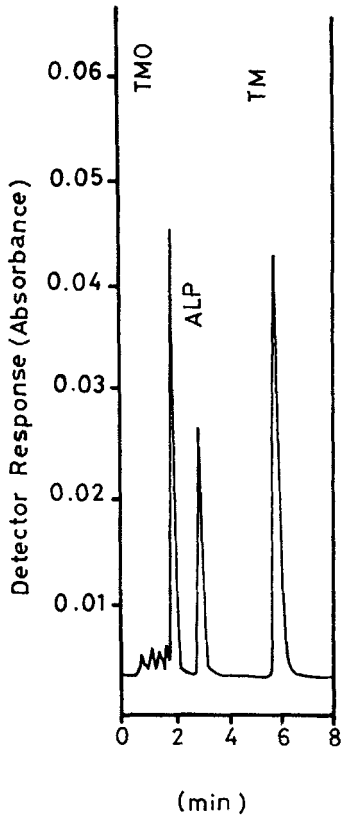

Figure 5: Chromatogram of triflupromazine-HCl (TM), triflupromazine-sulphoxide (TMO) and alprenolol (ALP) as internal standard. AUFSD = 0.1, 10 µL injected. Retention times are 6.1, 2.0 and 3.2 minutes for TM, TMO and ALP respectively. UV-detection at 254 nm, mobile phase flow rate 1.2 mL/min.

concentration, was determined for each compound by comparing test results from samples of known concentration of analyte with those of blank samples taking 3:1 as the signal-to-noise ratio.

To assess the reproducibility of the proposed HPLC system, at least six replicate 10 µL injections of standard solutions for each of perphenazine, trifluoperazine and triflupromazine and their sulphoxides were performed at

Table 1

The Chromatographic Parameters Established by RP-HPLC

C': *P'	PRO & PRO	TF & TFO	TM & TMO
Retention time (t_R) in minute	4.4 (PR) 1.7 (PRO) 2.5 (PI)	5.5 (TF) 1.8 (TFO) 3.4 (ALP)	6.1 (TM) 2.0 (TMO) 3.2 (ALP)
Capacity factor (k')	3.8 (PR) 1.12 (PRO) 2.2 (PI)	4.3 (TF) 1.2 (TFO) 2.5 (ALP)	4.6 (TM) 1.28 (TMO) 2.78 (alp)
Resolution (Rs)	3.7 (PR-PI) 1.82 (PRO-PI)	2.15 (TF-ALP) 2.28 (TFO-ALP)	4.1 (TM-ALP) 1.97 (TMO-ALP)
Column efficiency (N) plate/m	21333	20983	19987
Selective factor (α) (=k'_2/k'_1)**	1.70	1.72	1.65
Tailing factor, at 10%	1.20 (PR)	1.12 (TF)	1.25 (TM)

PR = Perphenazine, PR = Perphenazine sulphoxide.
TF = Trifluoperazine, TFO = Trifluoperazine sulphoxide.
TM = Triflupromazine, TMO = Triflupromazine sulphoxide.
PI Pindolol and (ALP) Alprenolol are internal standards.
*P' = Chromatographic Paramers, C' = Compound.
**refers to capacity factors for the parent phenothiazine and the internal standard.

low, medium and high concentrations of their linear ranges. The relative standard derivation (RSD) in all cases was less than 2% [Table 2 (c)], suggesting adequate reproducibility.

To examine the interday and intraday precision of the proposed HPLC method, as a measure of its ruggedness, a two-way analysis of variance (ANOVA) was performed using five replicates average peak-area ratios of

Table 2

The Parameters of the Standard Curves Using the Proposed HPLC Method (a), the Linear Regression equations, (b) and the Reproducibility Measured by R.S.D. %, (c)

Part (a)

Average Peak Area Response Ratios (Y)

PR/is	PRO/is	TF/is	TFO/is	TM/is	TMO/is
0.610	0.460	0.602	0.217	0.668	0.247
1.210	0.920	1.210	0.324	1.327	0.490
1.810	1.390	1.800	0.434	2.009	0.741
2.420	1.840	2.410	0.542	2.675	0.997
3.060	2.370	3.000	0.648	3.279	1.229
3.630	2.740	3.610	0.760	3.970	1.478
				4.680	1.719
				5.308	1.954

Part (b)

Regression equation Y = A + BC

C' P'	PR	PRO	TF	TFO	TM	TMO
A	-2.667×10^{-2}	0.000	3.333×10^{-3}	-4.286×10^{-4}	-3.773×10^{-3}	-6.679×10^{-3}
B	0.607	0.241	0.3000	0.054	0.664	0.1222
r	0.9999	0.9994	1.0000	1.0000	0.9999	0.9999
R	0.5-6	0.5-12	1-12	2-14	1-10	1-6
n	6	6	6	6	6	6
D.L.	0.1	0.2	0.15	0.15	0.1	0.2

(continued)

Table 2 (continued)

The Parameters of the Standard Curves Using the Proposed HPLC Method (a), the Linear Regression equations, (b) and the Reproducibility Measured by R.S.D. %, (c)

Part (c)

Reproducibility, R.S.D. %

C' / C	PR	PRO	TF	TFO	TM	TMO
Low	1.37	1.83	0.58	0.59	0.42	1.37
Medium	1.08	1.20	1.54	0.46	0.23	0.32
High	0.91	0.54	0.97	0.35	0.75	1.26

PR = Perphenazine, PR = Perphenazine sulphoxide.
TF = Trifluoperazine, TFO = Trifluoperazine sulphoxide.
TM = Triflupromazine, TMO = Triflupromazine sulphoxide.
is = Internal standard
A = Intercept
B = Slope
n = Number 0f determination
C = Concentration
D.L. = Lower detection limit in ng.
C' = Compound
R = Range of concentration in μgmL^{-1}
P' = Parameter
r = Correlation coefficient

medium concentration for each compound for five consecutive days. Typical ANOVA results for trifluoperazine dihydrochloride and its sulphoxide are displayed in Tables 3 (a, b). It is evident that at 95% confidence level, the tabulated variance ratios (F) at the specified degrees of freedom are greater than those observed with regard to between- and within-days variations. It can therefore be concluded that the precision is satisfactory based on the non-significant difference between the observed $F^{4,16}$ and the tabulated $F_{0.95}$.^{4,16}

To evaluate the accuracy of the proposed HPLC method, added recovery experiments were carried out by spiking known quantities of standard drug substance to the sample preparations. Typical and acceptable results for

Table 3 (a, b)

Two-way Analysis of Variance (ANOVA)

Part (a)
Daily Replicate Responses of 8 μg/mL Solution of Trifluoperazine 2HCl (TFO) and Two-way ANOVA

Day				
1	**2**	**3**	**4**	**5**
0.41	0.44	0.42	0.44	0.43
0.42	0.42	0.44	0.43	0.42
0.44	0.43	0.42	0.41	0.44
0.42	0.43	0.44	0.43	0.42
0.45	0.41	0.42	0.43	0.43

Part (b)
Daily Replicate Responses of 4μg/mL Solution of Triflupormazine Hcl (TM) and Two-way ANOVA

Day				
1	**2**	**3**	**4**	**5**
2.70	2.68	2.67	2.71	2.69
2.69	2.71	2.68	2.67	2.70
2.68	2.67	2.70	2.69	2.68
2.70	2.69	2.68	2.71	2.67
2.67	2.70	2.69	2.68	2.69

Source of Variation	**Degree of Freedom**	**Sum of Squares**	**Mean of Square**
Between days:	4	1.831055×10^{-4}	4.577637×10^{-5}
Within days:	4	2.136231×10^{-4}	5.340576×10^{-5}
Error	16	3.808699×10^{-3}	2.380437×10^{-4}
Total	24	4.205427×10^{-3}	

-Observed $F^{4,16}$ for between days variation = 0.1923024
-Observed $F^{4,16}$ for within days variation = 0.22243528
-Tabulated $F_{0.95}{}^{4,16}$ for the analytical error = 3.06

Table 4

Results of Determinations of Perphenazine (Trilafon®-4mg), Trifluoperazine 2HCL (Stelazine®-5mg) Tablets and Added Recovery Experiments by the Proposed HPLC Method

Perphenazine Tablets		Trifluoperazine Tablets	
mg/Tablet Found	%Added Recovery	mg/Tablet Found	%Added Recovery
3.97	97.7	4.94	98.3
4.00	99.1	4.98	98.0
4.05	99.8	4.94	98.8
4.08	100.1	4.92	99.2
4.05	100.4	4.93	100.0
4.05	99.7	4.91	100.5
4.06	----	4.92	----
4.06	----	----	----
4.01	----	----	----
4.00	----	----	----
****4.03	99.6%	****4.94	99.1%
***±0.04	±0.6%	***±0.023	±1.0%
**±0.88%	----	±0.46%	----
*4.03 ± 0.025	----	*4.94 ± 0.21	----

**** Mean mg per tablet
*** Standard deviation
** Relative standard deviation
* True mean at 95% confidence level

recovery experiments using perphenazine and trifluoperazine tablets were 99.6% ± 0.6 and 99.1% ± 1.0, respectively (Table 4).

CONCLUSION

The results summarized in Tables (5, 6 and 7) indicate that the elaborated HPLC method, unlike the BP[20] method, is capable of quantitating precisely and accurately perphenazine and trifluoperazine and their coexisting sulphoxides. The results obtained by the BP method are clearly for total recovered quantities of the parent compound and its sulphoxide. The BP method for the assay of the

Table 5

Results of the Analysis of Perphenazine and Its Sulphoxide

Part (a)

Results of the Analysis of PR & PRO Synthetic Mixture by the Proposed HPLC and BP Methods

Proposed HPLC Method				BP Method	
C. of PR μg/ml	C of PRO μg/ml	% m/m PRO:PR	% of PR recovered	% of PRO recovered	% of total recovered as PR
80	20	25.00	98.56	99.95	108.10
90	10	11.11	99.00	99.60	107.56
190	10	5.26	98.98	99.50	107.20
495	5	1.01	99.01	98.60	106.60
497.5	2.5	0.50	99.50	97.60	105.40
997.5	2.5	0.25	99.80	96.40	102.98

Part (b)

Results of the Analysis of PR Tablets Powder Spiked With PRO by the Proposed HPLC and BP Methods

Proposed HPLC Method				BP Method	
C. of PR μg/ml	C of PRO μg/ml	% m/m PRO:PR	% of PR recovered	% of PRO recovered	% of total recovered as PR
80	20	25.00	98.10	99.00	107.88
90	10	11.11	98.50	98.80	107.00
190	10	5.26	98.20	98.20	106.80
495	5	1.01	97.98	98.00	06.20
497.5	2.5	0.50	99.99	97.60	105.10
997.5	2.5	0.25	99.40	96.40	104.00

PR = Perphenazine
PRO = Perphenazine sulphoxide
C = Concentration

Table 6

Results of the Analysis of Trifluoperazine. 2HCl and its Sulphoxide

Part (a)

Results of the Analysis of TF & TFO Synthetic Mixture by the Proposed HPLC and BP Methods

Proposed HPLC Method				BP Method	
C. of PR μg/ml	C of PRO μg/ml	% m/m PRO:PR	% of PR recovered	% of PRO recovered	% of total recovered as TF
80	20	25.00	98.88	99.20	110.90
90	10	11.11	96.40	99.10	109.20
190	10	5.26	97.40	98.80	107.60
495	5	1.01	98.80	97.00	105.80
497.5	2.5	0.50	98.70	96.00	104.70
997.5	2.5	0.25	99.00	95.20	102.90

Part (b)

Results of the Analysis of TF Tablets Powder Spiked With TFO by the Proposed HPLC and BP Methods

Proposed HPLC Method				BP Method	
C. of PR μg/ml	C of PRO μg/ml	% m/m PRO:PR	% of PR recovered	% of PRO recovered	% of total recovered as TF
80	20	25.00	95.00	98.90	109.00
90	10	11.11	95.80	98.60	108.60
190	10	5.26	96.95	98.50	108.10
495	5	1.01	98.00	96.80	106.99
497.5	2.5	0.50	98.20	96.40	106.00
997.5	2.5	0.25	98.60	95.80	104.50

TF = Trifluoperazine. 2HCL
TFO = Trifluoperazine sulphoxide
C = Concentration

Table 7

Results of the Analysis of TM & TMO Synthetic Mixture by the Proposed HPLC Method

Proposed HPLC Method

C. of PR μg/mL	C. of PRO μg/mL	% m/m PRO:PR	% of PR recovered	% of PRO recovered
80	20	25.00	95.88	99.60
90	10	11.11	96.67	99.40
190	10	5.26	98.00	99.00
495	5	1.01	98.99	96.00
497.5	2.5	0.50	99.99	95.80
997.5	2.5	0.25	99.80	95.00

TM = Triflupormazine. HCl
TMO = Triflupormazine sulphoxide
C = Concentration

tablets is a spectrophotometric procedure which measures the absorbance of the two compounds additively, and hence the content per tablet will be for total recovered as parent compound. The superiority of the elaborated HPLC method over that of the BP stems from the ability of the former to separate and then quantitate.

It can be seen from Tables 5 and 6 that the elaborated HPLC method is sensitive to low levels of sulphoxide since accurate results can be achieved down to 0.25% m/m contamination. The sensitivity can be improved further if fluorometric or electrochemical rather than UV detection is used.

The results obtained for triflupromazine (USP official drug) in synthetic mixtures, (Table 7) confirm the suitability of the HPLC method for accurate and precise determination of triflupromazine sulphoxide in the presence of the parent compound.

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