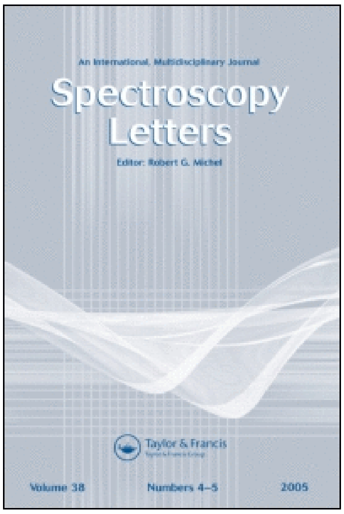


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Determination of Promethazine Hydrochloride with Palladium(II) and Na_2WO_4 by Resonance Rayleigh Scattering and Resonance Nonlinear Scattering Spectra

Pei-Li Chen[a]; Shao-Pu Liu[a]; Zhong-Fang Liu[a]; Xiao-Li Hu[a]
[a] Key Laboratory on Luminescence and Real-Time Analysis, Ministry of Education, School of Chemistry and Chemical Engineering, Southwest University, Chongqing, China

To cite this Article Chen, Pei-Li , Liu, Shao-Pu , Liu, Zhong-Fang and Hu, Xiao-Li(2010) 'Determination of Promethazine Hydrochloride with Palladium(II) and Na_2WO_4 by Resonance Rayleigh Scattering and Resonance Nonlinear Scattering Spectra', Spectroscopy Letters, 43: 6, 491 — 499

To link to this Article: DOI: 10.1080/00387010903360321

URL: http://dx.doi.org/10.1080/00387010903360321

Spectroscopy Letters, 43:491–499, 2010
Copyright © Taylor & Francis Group, LLC
ISSN: 0038-7010 print/1532-2289 online
DOI: 10.1080/00387010903360321

Taylor & Francis
Taylor & Francis Group

Determination of Promethazine Hydrochloride with Palladium(II) and Na_2WO_4 by Resonance Rayleigh Scattering and Resonance Nonlinear Scattering Spectra

Pei-Li Chen,
Shao-Pu Liu,
Zhong-Fang Liu,
and Xiao-Li Hu

Key Laboratory on Luminescence and Real-Time Analysis, Ministry of Education, School of Chemistry and Chemical Engineering, Southwest University, Chongqing, China

ABSTRACT In a weak acidic medium, promethazine hydrochloride (PMZ) reacted with Pd(II) to form 2:1 cationic chelate ($[Pd(PMZ)_2]^{2+}$), it further reacted with Na_2WO_4 by virtue of electrostatic attraction and hydrophobic force to form 1:1 ternary ion-association complex ($[Pd(PMZ)_2]\cdot(WO_4)$), which can result in the large-scale enhancement of the resonance Rayleigh scattering (RRS), second-order scattering (SOS) and frequency doubling scattering (FDS). The maximum RRS, SOS and FDS peaks of $[Pd(PMZ)_2]\cdot(WO_4)$ were located at 310 nm, 570 nm and 391 nm, respectively, and the enhancements of scattering were proportional to the concentration of PMZ in the range of 0.0081–2.6 $\mu g\,mL^{-1}$ (RRS method), 0.02–3.0 $\mu g\,mL^{-1}$ (SOS method) and 0.08–2.6 $\mu g\,mL^{-1}$ (FDS method). Above three methods' detection limits (3σ) were 2.1 $ng\,mL^{-1}$, 4.4 $ng\,mL^{-1}$ and 6.6 $ng\,mL^{-1}$ respectively. Using Pd(II) and Na_2WO_4 as probe, we have developed three new, sensitive, and rapid methods for the determination of PMZ. The RRS method was applied in the determination of PMZ in the pharmaceutical form with satisfactory results. In this work, the optimal reaction conditions and the influences of coexisting substances were investigated, the composition of ion-association complex and the reaction mechanism were also discussed by the RRS method.

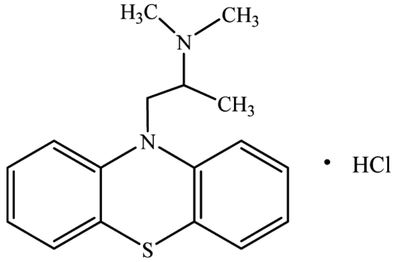
KEYWORDS Na_2WO_4, palladium(II), promethazine hydrochloride, resonance Rayleigh scattering, second-order scattering, frequency doubling scattering

Received 31 August 2009;
accepted 23 September 2009.

Address correspondence to Xiao-Li Hu, Key Laboratory on Luminescence and Real-Time Analysis, Ministry of Education, Chongqing 400715, China. E-mail: xiaolihu@swu.edu.cn

INTRODUCTION

Promethazine hydrochloride is the generic name of 10-N,N-dimethyl-1-(10H-phenothiazin-10-yl) propan-2-amine hydrochloride (Scheme 1). It is one of the most prominent phenothiazine derivatives, and is mainly used as the histamine H1-receptor antagonist and antiemetic for the symptomatic



SCHEME 1 The structure of PMZ.

relief of hypersensitivity reactions or for enhancing the analgesic, anesthetic, and sedative effects.[1,2] Due to its biomedical significance and global consumption of promethazine, more and more researchers search to establish many official and non-official standard methods for its determination.

Many official and other non-official standard methods have been used for the determination of PMZ such as spectrophotometry (SP),[3–10] high performance liquid chromatography (HPLC),[11–14] electrochemical method,[15–17]capillary electrophoresis (CE),[18,19] sequential injection analysis (SIA)[20] and flow-injection chemiluminescence (FIA-CL)[21,22] etc. But there are more or less pitfalls above methods. The official methods listed in BP[3] for phenothiazines include potentiometric titrimetry or spectrophotometry in the ultraviolet region, depending on the derivative. So time-consuming is required by the titrimetry and care must be taken with the spectrophotometry since many organic compounds absorb in this region of the spectrum. In the USP[4] method, it is assayed in tablets also spectrophotometrically but the method is far longer and more reagent-consuming than the BP method since it implies lengthy extraction and consuming many reagents. The non-official methods such as SP, HPLC, CE, SIA, FIA-CL etc, are also defects. Most spectrophotometric methods are lengthy and less selective. The HPLC technique is high selective and sensitive, but the costs of the equipment, its maintenance, solvent consumption, and disposal are high. Other methods such as FIA-CL, CE, SIA etc, based on the measurement of the absorbance of the oxidized form of promethazine suffered from accuracy and reproducibility, since the oxidized form of promethazine is unstable and requires a rapid and fully automated handling technique. In a word, the majority of the offered methods for the determination of PMZ were not optimized. Hence it is important to find a more efficient method for determination of PMZ.

Because of their high sensitivities, accuracy, and low outlay, new analytical techniques of RRS, SOS, and FDS have been applied in the determination of nucleic acids,[23] proteins,[24–28] and some drugs.[29–37]

Our experiments found that at room temperature and pH 4.6–5.3 Britton-Robinson (BR) buffer medium, Pd(II) reacted with PMZ to form 1:2 cationic chelate $[Pd(PMZ)_2]^{2+}$, which further reacted with Na_2WO_4 to form a 1:1 ternary ion-association complex $([Pd(PMZ)_2]\cdot(WO_4))$ and RRS, SOS, FDS were increased rapidly. The maximum RRS, SOS, and FDS wavelengths of ternary ion-association complex were located at 310 nm, 570 nm and 391 nm, respectively. The enhancements of scattering were proportional to the concentration of PMZ in a certain range. So, above three methods all can determinate PMZ selectively. Their sensitivities are very high and the smallest detection limit (3σ) is 2.1 ng mL^{-1}. The sensitivities of three methods are not only higher by 1 to 3 orders of magnitude than common SP,[3–10] but also higher than many HPLC,[11–14] FIA-CL,[21,22] CE,[18,19] and SIA.[20] So they are more suitable for the determination of trace PMZ. This work investigated the ternary ion-association complex by RRS, SOS, and FDS methods. Because the sensitivity of the RRS method is higher than those of SOS and FDS, the optimal conditions and the influe, factors of the reaction by RRS method were our main focus. The effects of foreign substances were investigated and showed that the RRS method has a high selectivity. A simple, sensitive, and rapid method has been developed for the determination of PMZ in PMZ tablets. We also discuss the mechanism the ternary ion-association reaction and the reasons for RRS enhancement.

EXPERIMENTAL

Apparatus and Reagents

A Hitachi F-2500 spectroflurophotometer (Tokyo, Japan) was used to record the RRS and fluorescence spectra and to measure the scattering and fluorescence intensities. A UV-8500 spectrophotometer (Tianmei, Shanghai) was used to record the absorption spectra and to measure absorbance intensity. A PHS-3C pH meter (Shanghai Dazhong Analytical Instrument Plant) was used to adjust pH value.

The concentration for stock solution of PMZ (Chongqing Xi'nan Pharmaceutical Company, China) was 100.0 μg mL^{-1}, and the concentration for working solution was 10.0 μg mL^{-1}.

The concentration for working solution of Pd(II) (2.0×10^{-4} mol L^{-1}) (Shanghai Reagent First Plant) was prepared by dissolving 0.0187 g of $PdCl_2$ in 1.0 mL of concentrated HCl. The solution was cooled and diluted with water in a 250.0 mL calibrated flask. The concentration for working solutions of Na_2WO_4 was 5.0×10^{-4} mol L^{-1}. BR buffer solutions with different pH values were prepared according to suitable proportion and adjusted pH values with a pH meter. All reagents were analytical reagent grade, and doubly distilled water was used.

General Procedure

A 1.0 mL of pH 5.0 BR buffer solution was pipetted into a 10.0 mL calibrated flask followed by 1.0 mL 2.0×10^{-4} mol L^{-1} Pd(II) solution, suitable amounts of PMZ solution and 1.4 mL 5.0×10^{-4} mol L^{-1} Na_2WO_4 solution. The solution was diluted to the mark with water and shaker thoroughly, then set aside for 5.0 min. The RRS intensity (I^{RRS}) of the system was recorded with synchronous scanning at $\lambda_{ex} = \lambda_{em}$. The SOS intensity ($I^{SOS}$) and the FDS intensity (I^{FDS}) of the system were recorded at $\lambda_{em} = 2\lambda_{ex}$ and $2\lambda_{em} = \lambda_{ex}$, respectively. The I^{SOS} and I^{FDS} were plotted versus the different wavelengths to obtain SOS and FDS spectra. Then, the scattering intensities (I^{RRS}, I^{SOS} and I^{FDS}) for the ion-association complex, and I_0^{RRS}, I_0^{SOS} and I_0^{FDS} for the reagent blank at their own maximum were measured, $\Delta I^{RRS} = I^{RRS} - I_0^{RRS}$, $\Delta I^{SOS} = I^{SOS} - I_0^{SOS}$ and $\Delta I^{FDS} = I^{FDS} - I_0^{FDS}$.

RESULTS AND DISCUSSION

RRS Spectra

The RRS spectra of PMZ-Pd(II)–Na_2WO_4 system is shown in Fig. 1. From Fig. 1a, it can be seen that the RRS intensities of Na_2WO_4, Pd(II) and PMZ themselves are very weak. The binary chelate that Pd(II) and PMZ formed can only result in a little certain change of the RRS spectra. When the binary chelate further reacted with Na_2WO_4 to form ternary ion-association complex, RRS intensity was enhanced greatly. The maximum RRS peak was at 310 nm.

Figure 1b shows that the enhancement of RRS intensities for the PMZ-Pd(II)–Na_2WO_4 system was directly proportional to the concentration of PMZ. Hence, the RRS method can be applied to the determination of PMZ.

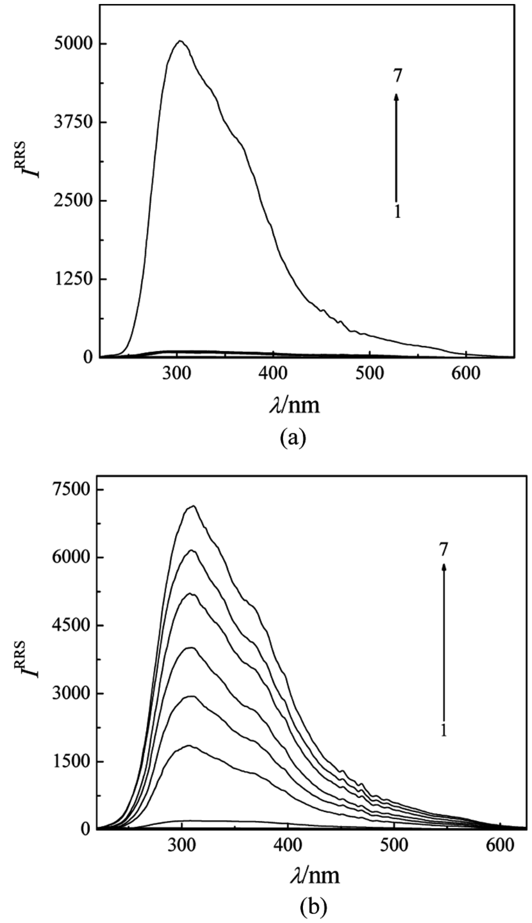


FIGURE 1 RRS spectra. (a) 1. Na_2WO_4; 2. PMZ; 3. Pd(II); 4. Pd(II)–Na_2WO_4; 5. PMZ-Pd(II); 6. PMZ–Na_2WO_4; 7. PMZ-Pd(II)–Na_2WO_4; concentration of PMZ: 1.8 μg mL^{-1}; concentration of Pd(II): 2.0×10^{-5} mol L^{-1}; concentration of Na_2WO_4: 7.0×10^{-5} mol L^{-1}. (b) Concentration of PMZ (1–7): 0, 0.6, 1.0, 1.4, 1.8, 2.2, 2.6 μg mL^{-1}; concentration of Pd(II): 2.0×10^{-5} mol L^{-1}; concentration of Na_2WO_4: 7.0×10^{-5} mol L^{-1}.

SOS Spectra

The SOS spectra of PMZ-Pd(II)–Na_2WO_4 system is shown in Fig. 2. From Fig. 2a, it can be seen that the SOS intensities of Na_2WO_4, Pd(II) and PMZ themselves are very weak. The binary chelate that Pd(II) and PMZ formed can only result a certain change of the SOS spectra. When the binary chelate further reacted with Na_2WO_4 to form ternary ion-association complex, SOS intensity was enhanced greatly. The maximum SOS peak was at 570 nm.

When the λ_{ex} was at 285 nm, the changes of SOS intensities with different concentration of PMZ were investigated (Fig. 2b). It can be seen from Fig. 2b that

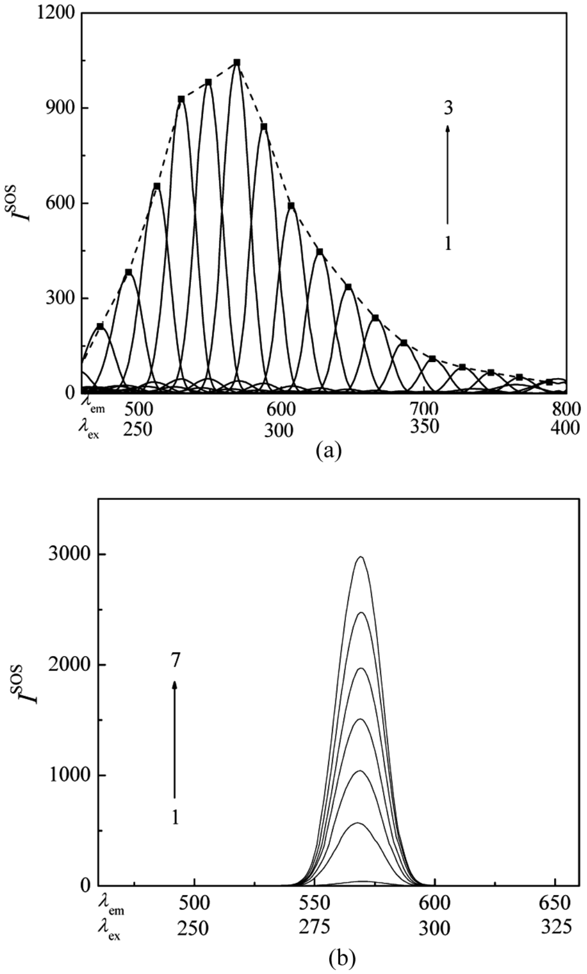


FIGURE 2 SOS spectra. (a) 1. PMZ; 2. PMZ-Pd(II); 3. PMZ-Pd(II)–Na_2WO_4; Dash line: whole SOS spectra. Concentration of PMZ: $1.0\,\mu g\,mL^{-1}$; concentration of Pd(II): $2.0 \times 10^{-5}\,mol\,L^{-1}$; concentration of Na_2WO_4: $7.0 \times 10^{-5}\,mol\,L^{-1}$. (b) Concentration of PMZ (1–7): 0, 0.5, 1.0, 1.5, 2.0, 2.5, $3.0\,\mu g\,mL^{-1}$; concentration of Pd(II): $2.0 \times 10^{-5}\,mol\,L^{-1}$; concentration of Na_2WO_4: $7.0 \times 10^{-5}\,mol\,L^{-1}$.

the enhancement of SOS intensity for system is linear to an increased concentration of PMZ. Hence, the SOS method can be applied to the determination of PMZ.

FDS Spectra

The FDS spectra of PMZ-Pd(II)–Na_2WO_4 system is shown in Fig. 3. From Fig. 3a, it can be seen that the FDS intensities of Na_2WO_4, Pd(II) and PMZ themselves are very weak. The binary chelate led to a certain change of the FDS spectra. When the binary chelate further reacted with Na_2WO_4 to form ternary ion-association complex, FDS intensity was enhanced greatly. The maximum FDS peak was at 391 nm.

When the λ_{ex} was at 782 nm, the changes of FDS intensities with different concentration of PMZ were investigated (Fig. 3b). It can be seen from Fig. 3b that the enhancement of FDS intensity for system is linear to an increased concentration of PMZ. So, the FDS method can be applied to the determination of PMZ.

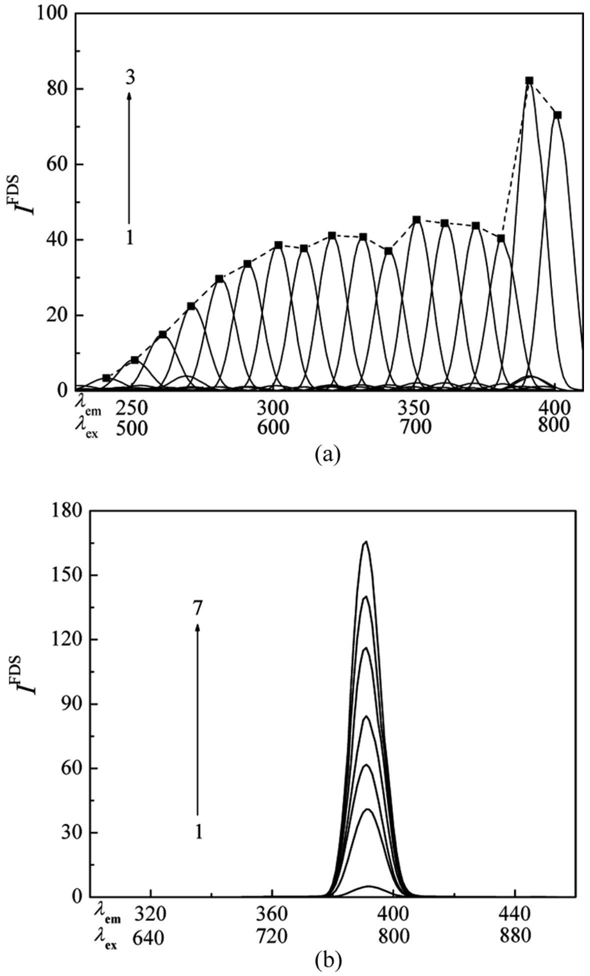


FIGURE 3 FDS spectra. (a) 1. PMZ; 2. PMZ-Pd(II); 3. PMZ-Pd(II)–Na_2WO_4; Dash line: whole FDS spectra. Concentration of PMZ: $1.4\,g\,mL^{-1}$; concentration of Pd(II): $2.0 \times 10^{-5}\,mol\,L^{-1}$; concentration of Na_2WO_4: $7.0 \times 10^{-5}\,mol\,L^{-1}$. (b) Concentration of PMZ (1–7): 0, 0.6, 1.0, 1.4, 1.8, 2.2, $2.6\,\mu g\,mL^{-1}$; concentration of Pd(II): $2.0 \times 10^{-5}\,mol\,L^{-1}$; concentration of Na_2WO_4: $7.0 \times 10^{-5}\,mol\,L^{-1}$.

Because the sensitivity of RRS method is higher than those of SOS and FDS, the optimal conditions of the reactions, the properties of analytical chemistry and analytical applications by RRS method were investigated mainly.

Optimum Conditions

Effects of Acidity

The influences of different buffer solutions on RRS intensities of the reaction were tested with BR, HAc-NaAc and Citrate Sodium-HCl. The results showed that BR was better than other buffer solutions and the optimum pH range of reaction was 4.6 to 5.3 (Fig. 4). The RRS intensities would decrease if the acidity is over the range. When the acidity is too low, the WO_4^{2-} can combine with H^+ to form $[HW_6O_{21}]^{5-}$ by the polymerization reaction.[38] Thus the amount of WO_4^{2-} which react with $[Pd(PMZ)_2]^{2+}$ decreased and the reaction of $[Pd(PMZ)_2]^{2+}$ with WO_4^{2-} would be incomplete. When the acidity is too high, PMZ would protonate to form $HPMZ^+$. The coordination of PMZ to Pd^{2+} would weaken owing to mutual repulsion between $HPMZ^+$ and Pd^{2+}. So, pH 5.0 was chosen as reaction acidity for the system and the appropriate amount was 1.0 mL.

Effects of the Pd (II) Concentration

The experiment showed that RRS intensity reached the maximum and retained stability when the concentration of Pd(II) was from 1.0×10^{-5} mol L^{-1} to 3.0×10^{-5} mol L^{-1}. So the experiment concentration was 2.0×10^{-5} mol L^{-1} for Pd(II).

Effects of the Na_2WO_4 Concentration

The influences of the concentrations of Na_2WO_4 on the RRS intensity were investigated. The result showed that the RRS intensity enhanced gradually with the increasing of Na_2WO_4 concentration. When the concentration of Na_2WO_4 was from 5.0×10^{-5} mol L^{-1} to 9.0×10^{-5} mol L^{-1}, ΔI^{RRS} retained stability. If Na_2WO_4 was not enough, the reaction would be incomplete. If Na_2WO_4 was excessive, ΔI^{RRS} would decrease. So, 7.0×10^{-5} mol L^{-1} was chosen as suitable Na_2WO_4 concentration.

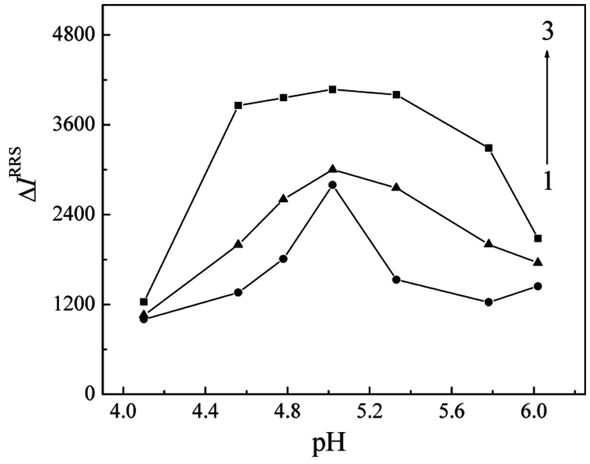


FIGURE 4 Effect of acidity. 1. HAc-NaAc; 2. Citrate Sodium-HCl 3. BR; concentration of Pd(II): 2.0×10^{-5} mol L^{-1}; concentration of Na_2WO_4: 7.0×10^{-5} mol L^{-1}; concentration of PMZ: 1.5 µg mL^{-1}.

Reaction Speed and the Stability

At room temperature, the reaction completed in 5.0 min and RRS intensity can remain constant for 1.5 h at least.

Sensitivities of Methods

Under the optimum experimental conditions, the different concentrations of PMZ reacted with Pd(II) and Na_2WO_4 to form ternary ion-association complex and the relative scattering intensities ΔI^{RRS}, ΔI^{SOS} and $\Delta I^{FDS}$of the ternary complex were measured at their maximum scattering wavelengths after 5.0 min. The calibration graphs of ΔI^{RRS}, ΔI^{SOS} and ΔI^{FDS} against the concentrations of PMZ were constructed. The correlation parameters were listed in Table 1. From Table 1, it can be seen that the sensitivity of RRS method is higher than those of SOS and FDS methods though three methods all can be applied to determinate PMZ. The detection limit (3σ) of PMZ by RRS method is 2.1 ng mL^{-1} for the system. RRS method has much higher sensitivity than other common analytical methods (Table 2). From Table 2, we can see that the sensitivities of three methods are not only higher by 1 to 3 orders of magnitude than common SP,[3–10] but also higher than many HPLC,[11–14] FIA-CL,[21,22] CE,[18,19] and SIA.[20] So they are more suitable for the determination of trace PMZ.

Formation of Ternary Ion-Association Complex and Its Effect on the Spectral Characteristics

The Ion-Association Reaction

We studied the ion-association reaction of PMZ with Pd(II) and Na_2WO_4. The composition ratio of the binary chelate for the Pd(II)-PMZ was 1:2 and the ternary complex was 1:2:1 as established by using Job's method of continuous variation and molar ratio method.

The ternary ion-association was $[Pd(PMZ)_2]^{2+}$ WO_4^{2-} and its structure was shown in Scheme 2, and the reaction mechanism was shown as follows: There are lone electron pairs in sulfur atom in the tricyclic structure of promethazine hydrochloride. Based on above characteristics, Pd(II) reacted with sulfur atom of PMZ to form 1:2 red complex compound by virtue of coordinate-covalent bond, which

TABLE 1 **Analytical Parameters for the Determination of PMZ**

Method	$\lambda_{ex}/\lambda_{em}$ (nm)	Linear range ($\mu g\,mL^{-1}$)	Regression equation (c, $\mu g\,mL^{-1}$)	Correlation coefficient (r)	Detection limit (3σ, $ng\,mL^{-1}$)
RRS	310/310	0.008–2.6	$\Delta I = 69.0 + 2668.9\ c$	0.9995	2.1
SOS	285/570	0.02–3.0	$\Delta I = 24.2 + 961.6\ c$	0.9998	4.4
FDS	782/391	0.08–2.6	$\Delta I = -5.3 + 63.6\ c$	0.9984	6.6

TABLE 2 **Comparison of the Sensitivities of RRS with Other Methods for the Determination of PMZ**

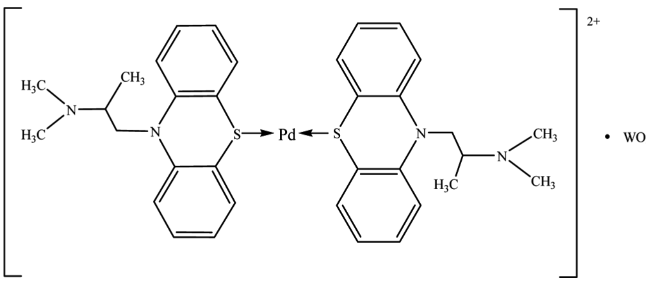
Method	Analytical reagent	Medium condition	Determination wavelength (nm)	Detection Limit (3σ, $\mu g\,mL^{-1}$)	Reference
HPLC		PH = 3.0 (KH_2PO_3)	249	0.02	[12]
			258	3.45	[13]
			306	11.62	[14]
FIA-CL	$Ce(SO_4)_2$	1.0 mol/L HCl		0.05	[21]
	$KMnO_4$-$C_2H_2O_2$	1.0 mol/L H_2SO_4		0.035	[22]
CE	Cerium(IV)	pH = 8.0	254	3.3	[19]
	Ru(bpy)(3)(2+)		270	0.019	[18]
SIA	Cerium(IV)	0.38 mol/L H_2SO_4	514	22.57	[20]
SP	Eosin Y	pH = 3.0 NaAc-HCl	516	0.221	[8]
	Iron-thiocyanat	HCl	299	1.93	[9]
	KCN		480	0.089	[5]
			515	1	[10]
RRS	Pd(II)-Na_2WO_4	pH = 5.02	310	0.0021	This work
SOS	Pd(II)-Na_2WO_4	pH = 5.02	570	0.0044	This work
FDS	Pd(II)-Na_2WO_4	pH = 5.02	391	0.0066	This work

SIA: sequential injection analysis; CE: capillary electrophoresis; SP: spectrophotometry; HPLC: high performance liquid chromatography; FIA-CL: flow-injection chemiluminescence.

is recorded by the book.[39] In pH 4.6–5.3 BR buffer medium, $[PdPMZ_2]^{2+}$ can react with WO_4^{2-} to form a ternary ion-association complex through electrostatic attraction and hydrophobic force.

Effect on Absorption Spectrum

PMZ has certain absorption at UV region because there are two isolated conjugated systems in its molecule structure. Their maximum absorption wavelength (λ_{max}) is at 248 nm and 301 nm. When it reacted with Pd(II) to form the complex compound, the absorption peaks changed and their maximum absorption wavelength (line 2) violet-shifted to 216 nm ($\Delta\lambda = 32$ nm) and red-shifted to 317 nm ($\Delta\lambda = 16$ nm), respectively. Simultaneously, there was a new absorption peak appeared at about 418 nm. The sensitivities, however, were low. Their molar absorptivities were 3.37×10^4 ($\lambda = 216$ nm) L $mol^{-1}\,cm^{-1}$, 9.32×10^3 ($\lambda = 317$ nm) L $mol^{-1}\,cm^{-1}$ and 3.3×10^3 ($\lambda = 418$ nm) L $mol^{-1}\,cm^{-1}$ which have no advantages to determination of PMZ by spectrophotometry. When the binary complex compound reacted with Na_2WO_4 to form ternary ion-association complex, the absorption peaks changed into a big absorption band respectively, but the sensitivities were still not high. Fig. 5 shows the absorption spectra of PMZ-Pd(II)–Na_2WO_4 system. It can be seen that the formation of the ternary ion-association complex are also not available for establishing a sensitive spectrophotometric method for the determination of PMZ.



SCHEME 2 **The structure of ($[Pd(PMZ)_2] \cdot (WO_4)$).**

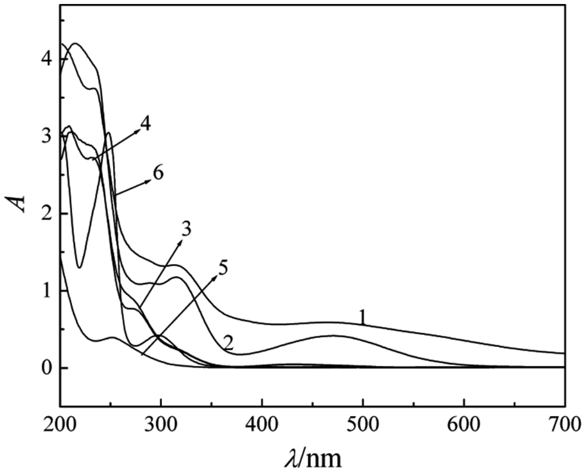


FIGURE 5 Absorption spectra for PMZ-Pd(II)–Na_2WO_4 system. 1. PMZ-Pd(II)–Na_2WO_4; 2. PMZ-Pd(II); 3. Pd(II)–Na_2WO_4 4. Pd (II); 5. Na_2WO_4; 6. PMZ; concentration of Pd(II): 1.0×10^{-4} mol L^{-1}; concentration of Na_2WO_4: 3.5×10^{-4} mol L^{-1}; concentration of PMZ: 40 μg mL^{-1}. Measured using a water blank.

Effect on RRS Spectra

It can be seen from above 3.1 that the formation of the ion-association complex resulted in great enhancement of RRS, SOS, and FDS. But the sensitivity of RRS method is higher than those of SOS and FDS methods. Therefore, RRS method is more suitable for the determination of trace amounts of PMZ.

The possible reasons for RRS enhancement included as follows: Resonance enhanced Rayleigh scattering effect. When the wavelength of Rayleigh scattering was located or was close to the molecular absorption band, the scattering can absorb the light energy through resonance to produce a rescattering process. As a result, the scattering intensity is greatly enhanced.[40,41] Figure 6 shows that the comparison of RRS spectra with absorption spectra. It can be seen from Figure 6 that the RRS spectra were located in its absorption band and one RRS peak 310 nm was close to corresponding one absorption peak 318 nm. Therefore, scattering intensity was remarkably increased due to the absorption of light and a re-scattering process. So the resonance enhanced effect is an important reason for scattering enhancement of the ternary ion-association complex system.

1. Enhancement of hydrophobicity:
   Pd(II), $[Pd(PMZ)_2]^{2+}$, and WO_4^{2-} all have hydrophility and can easily dissolved in aqueous solution so that they can't form an interface with water. When $[Pd(PMZ)_2]^{2+}$ reacted with WO_4^{2-} to form the neutral ternary ion-association complex ($[Pd(PMZ)_2] \cdot (WO_4)$), a hydrophobic liquid-solid interface appeared, owing to the presence of the hydrophobic aryl framework of the ternary complex. The formation of the hydrophobic interface is beneficial to the enhancement of the RRS signal.[42]

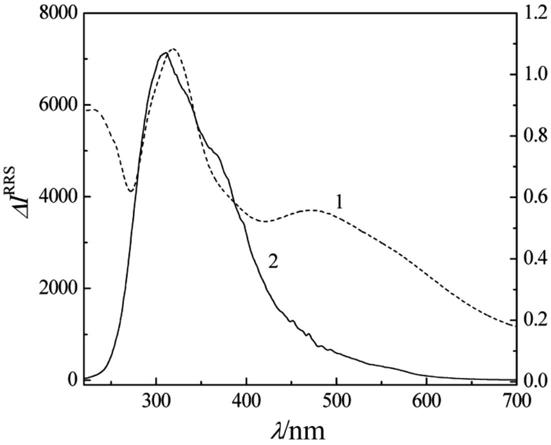


FIGURE 6 Comparison of RRS spectra and absorption spectra. 1. Absorption spectra (using a reagent blank); 2. RRS spectra.

2. Enlargement of molecular volume:
   It is known that the bigger of molecular volume, the higher of the RRS intensity when other parameters are invariable. If molecular volume is not easy to calculate, it can be substituted by molecular weight. i.e., $I = KCMI_0$.[43] When the binary chelate $[Pd(PMZ)_2]^{2+}$ reacted with Na_2WO_4 to form the ternary complex $[Pd(PMZ)_2] \cdot (WO_4)$, the molecular weights increased from 320.89 to 995.98. The increase of the molecular volume (or weight) is a significant factor to the enhancement of RRS intensity.

Affected by all above factors, the RRS intensities of the productions enhanced notably.

Selectivity of RRS Method and Its Analytical Application Effect of Foreign Substances

Under optimal conditions, the effects of some coexisting substances on the determination were tested. Table 3 shows that few coexisting ions interfere with the determination of PMZ. When the concentration of PMZ was 1.0 μg mL^{-1}, 147.5–2047.5 times of common ions such as Na^+, K^+, Ba^{2+},

TABLE 3 Effect of Foreign Substances ($C_{PMZ} = 1.0\,\mu g\,mL^{-1}$)

Foreign substances	Concentration ($\mu g\,mL^{-1}$)	Change in I_{RRS} (%)	Foreign substances	Concentration ($\mu g\,mL^{-1}$)	Change in I_{RRS} (%)
Na^+, Cl^-	2047.5	−4.2	Maltose	550	2.4
K^+, I^-	1494	2.7	Starch	66.75	−0.75
Na^+, F^-	420	−2.6	Threonine	160	−1.5
Ba^{2+}, Cl^-	936	−0.2	DL-Arginine	18	0.84
Zn^{2+},CH_3COO^-	7.65	−3.5	L-Tyrosine	120	0.7
Cd^{2+-}, SO_4^{2-}	1.14	4.1	Glycin	180	−1.2
Cu^{2+}, SO_4^{2-}	60	−3.7	L-Tryptophan	46	−4.6
Co^{2+}, Cl^-	147.5	−2.7	DL-Aspartic	150	−2.2
Sr^{2+}, Cl^-	158.6	0.6	Urea	3000	−0.5
Na^+, SCN^-	19.8	−4.4	Pepsin	20	1.9
Saccharose	900	0.41	HSA	26	−2.1
Lactose	800	−1.8	BSA	13	−1.2

TABLE 4 Results for the Determination of PMZ in Tablets

Method	Found mean value (mg/one tablet, n = 5)	Specified amount (mg/one tablet)	Recovery (%) (n = 5)	RSD (%)
RRS	24.95	25.0	99.8	1.7
UV-spectrophotometry[43]	24.69	25.0	98.8	1.8

Co^{2+}, Sr^{2+}, Cl^-, I^-, F^-, SO_4^{2-}, 3000 times of urea, 13 to 26 times of BSA, HAS, pepsin, 18 to 160 times of amino acids and 550 to 900 times of saccharine do not interfere with determination, while Cd^{2+}, Zn^{2+}, CH_3COO^-, SCN^- were tolerated at a lower level. So the RRS method has a good selectivity and it can be applied to determination of PMZ.

Analytical Application

Fifteen units of PMZ tablets were shucked sugar-coating and weight, then ground to a fine power. A portion of the powder containing 25.0 mg of the active component was accurately weighed into a 100.0 mL calibrated flask, distilled water were added and agitated thoroughly. The solution was transferred into a 250.0 mL volumetric flask and diluted with water to the mark. A suitable aliquot of the diluted solution was analysed as described under general procedure. The results are shown in Table 4.

It can be seen from Table 4 that the RRS method has a good repeatability. The RSD of PMZ tablets is between 1.3% and 1.8% and the recovery of PMZ tablets is from 98.3% to 99.8%. Therefore, the method can be used for the determination of PMZ in PMZ tablets.

CONCLUSIONS

Based on the formation of the ion-association complex of PMZ-Pd(II) chelate with Na_2WO_4 by RRS, SOS and FDS techniques, we have developed a sensitive, rapid and simple method for the determination of PMZ. The proposed method was successfully applied to the determination of trace amounts of PMZ in PMZ tablets.

ACKNOWLEDGMENTS

The authors gratefully acknowledge financial support for this study by the National Natural Science Foundation of China (Grant No. 20875078) and Chongqing Municipal Key Laboratory on Luminescence and Real-Time Analysis (Grant No. CSTC 2006CA8006).

REFERENCES

1. British Pharmacopoeia, E-copy on CD, Ver. 6.0, 2002.
2. Basavaiah, K.; Manjunatha, J. M.; Krishnamurthy, G. Quantitation of pharmaceutically important phenothiazines by oxidimetry. *Il Farmaco* **2000**, *55*, 87–92.
3. British Pharmacopoeia, Her Majesty's Stationary Office, London, 1993.
4. United States Pharmacopoeia, E-copy on CD, Ver. 26-NF 21, 2003.
5. Tarasiewicz, M.; Kuzmicka, L. Determination of thioridazine by means of absorption spectrometry. *Pharmazie* **1996**, *51*, 189–190.

6. Basavaiah, K.; Swamy, J. M. Application of potassium dichromate and iron-thiocyanate in the spectrophoto metricinvestigations of phenothiazines. *Il Farmaco* **2001**, *56*, 579–585.
7. Regulska, E.; Tarasiewicz, M.; Puzanowska-Tarasiewicz, H. Extractive-spectrophotometric determination of some phenothiazines with dipicrylamine and picricacid. *J. Pharm. Biomed. Anal.* **2002**, *27*, 335–340.
8. Qin, Z. H.; Liu, S. P.; Kong, L.; Jing, H. Spectrophotometric determination of promethazine hydrochloride with eosin Y. *Chin. J. Anal. Chim.* **2003**, *31*(6), 702–705.
9. Luo, J. H.; Jiang, Y. G. Determination of Promethazinein Yekeling by Ultraviolet Spectrophotometry. *Anitin Infection Poharomal* **2006**, *3*(1), 30–31.
10. Saif, M. J.; Anwar, J. A new spectrophotometric method for the determination of Promethazine-HCl from pure and pharmaceutical preparation. *Talanta* **2005**, *67*, 869–872.
11. De Orsi, D.; Gagliardi, L.; Tonelli, D. High performance liquid chromatographic determination of prozapine in pharmaceutical formulations. *J. Pharm. Biomed. Anal.* **1996**, *14*, 1635–1638.
12. Liang, G. L.; Wang, X. Q.; Zhong, P. HPLC Determination of promethazine hydrochloride in phenothiazines and bile tablets. *Chin. J. Pharm. Anal.* **2005**, *25*(9), 1129–1131.
13. Chen, D. X. HPLC Determination of hlydrochlorothiazide, dibazol, chlordiazepoxide and promethazine hydrochloride in compound dibazol capsules. *Chin. J. Pharm. Anal.* **2005**, *25*(4), 442–445.
14. Chen, D. X.; Zhang, J. R. Determination the content of pediatric paracetamol promethazine tablets by HPLC. *Chin. JMAP.* **2008**, *25*(2), 133–135.
15. Zimová, N.; Nmec, I.; Zima, J. Determination of chlorpromazine and thioridazine by differential pulse voltammetry in acetonitrile medium. *Talanta* **1986**, *33*(6), 467–470.
16. Ni, Y.; Wang, L.; Kokot, S. Simple and sensitive fluorimetric liquid chromatography for simultaneous analysis of chenodiol and ursodiolin pharmaceutical formulations. *Anal. Chim. Acta* **2001**, *493*, 159–166.
17. Lima, J. L. F. C.; Motenogro, B. S. M.; Conceicao, M.; Goreti, F. S. M. Ion elective lectrode for promethazine determinationin in pharmaceutical preparation and application to flow injection analysis. *J. Pharm. Sci.* **1977**, *86*, 1234–1238.
18. Li, Y. H.; Wang, C. Y.; Tian, J.; Liu, X. Q.; You, T. Y. Separation and detection of chlorpromazine hydrochloride and promethazine hydrochloride using electrochemiluminescence followed by capillary electrophoresis. *Asian J. Chem.* **2008**, *20*(5), 3833–3848.
19. Francisco Lara, J.; Ana García-Campaña, M.; Fermín Alés-Barreroand Juan Bosque-Sendra, M. Determination of thiazinamium, promazine and promethazine in pharmaceutical formulations using a CZE method. *Anal. Chim. Acta* **2005**, *535*, 101–108.
20. Idris, A. M.; Assubaie, F. N.; Sultan, S. M. Chemometric optimization of a SIA promethazine hydrochloride assay method. *Microchem. J.* **2006**, *83*(1), 7–13.
21. Han, X. N.; Tang, Y. H.; Yu, C. L.; Wang, N. N.; Xiong, X. Y. The determination of phenothiazines by a flow-injection chemiluminescence method. *Chin. J. Pharm. Anal.* **2005**, *25*(12), 1527–1530.
22. Nie, Y. H.; He, Y. Y.; Feng, M. L.; lv, J. R. Determination of promethazine hydrochloride by flow-injection chemiluminescence detection. *Chin. J. Anal. Chim.* **1999**, *27*(4), 427–429.
23. Du, J.; Zheng, H. Z.; Huang, C. Z.; Wen, C. Y.; Hao, J. Y.; Hu, Y. F.; Zhou, D. B.; Liu, L. Positive charged polymer as a probe for DNA determination by resonance light scattering. *Anal. Sciences* **2009**, *25*(5), 727–730.
24. Li, L.; Song, G. W.; Fang, G. R. Determination of bovine serum albumin in the form of its triple complex with Fe(bpy)(phen)SO_4-Myristylpyridinium bromide by resonance light-scattering technique. *Chemia. Analityczna* **2009**, *54*(1), 99–107.
25. Lu, X.; Luo, Z. H.; Liu, C. W.; Zhao, S. L. Resonance Rayleigh scattering for detection of proteins in HPLC. *J. Separation Science* **2008**, *31*(16–17), 2988–2993.
26. Li, Y. F.; Shen, X. W.; Huang, C. Z. A coupled reagent of o-phthalaldehyde and sulfanilic acid for protein detection based on the measurements of light scattering signals with a common spectrofluorometer. *Talanta* **2008**, *75*(4), 1041–1045.
27. Long, X. F.; Zhang, C. H.; Cheng, J. J.; Bi, S. P. A novel method for study of the aggregation of protein induced by metal ion aluminum(III) using resonance Rayleigh scattering technique. *Spectrochim. Acta Part A* **2008**, *69*(1), 71–77.
28. Guo, Z. X.; Shen, H. X. Sensitive and simple determination of protein by resonance Rayleigh scattering with 4-azochromotropicacid phenylfluorone. *Anal. Chim. Acta* **2000**, *408*, 177–182.
29. Chen, Z. G.; Zhu, L.; Song, T. H.; Chen, J. H.; Guo, Z. M. A novel curcumin assay with the metalion Cu(II) as a simple probe by resonance light scattering technique. *Spectrochim. Acta Biomol. Spectro.* **2009**, *72*(3), 518–522.
30. Duan, H.; Liu, Z. F.; Hu, X. L.; Liu, S. P. Determination of penicillin antibiotics by resonance Rayleigh scattering method with KIO_3-KBr-methyl violet. *J. Southwest Univ. (Nat. Sci.)* **2008**, *30*(5), 31–35.
31. Fu, S. H.; Liu, Z. F.; Liu, S. P.; Yi, A. X. Study on the resonance Rayleigh scattering, second-order scattering and frequency doubling scattering spectra of the interactions of palladium(II)-ceftriaxone chelate with anionic surfactants and their analytical applications. *Talanta* **2008**, *75*, 528–535.
32. Yang, J. D.; Cao, T. W.; Liu, Z. F.; Kong, L.; Liu, S. P. Effects of the interaction of rifamycin SV with serum albumins on the resonance Rayleigh scattering spectra and their analytical application. *Chin. J. Chem.* **2008**, *26*(5), 893–897.
33. Meng, W. W.; Liu, Z. F.; Liu, S. P.; Hu, X. L.; Shi, Y. Hyper Rayleigh scattering spectra of palladium (II)-moroxydine hydrochloride-fluorescein halide dye systems and their analytical application. *J. Southwest Univ. (Nat. Sci.)* **2009**, *31*(4), 49–53.
34. Feng, S. L.; Liu, J. J.; Han, X. M.; Fan, J. Resonance light scattering study on the interaction of benproperine phosphate with eriochrome blue black R in the presence of sodium dodecylbenzene sulphonate and its analytical application. *Luminesecence* **2009**, *24*(2), 67–72.
35. Xi, C. X.; Liu, Z. F.; Kong, L.; Hu, X. L.; Liu, S. P. Effects of interaction of folic acid with uranium(VI) and basic triphenylmethane dyes on resonance Rayleigh scattering spectra and their analytical applications. *Anal. Chim. Acta* **2008**, *613*, 83–90.
36. Qin, M. Y.; Liu, S. P.; Liu, Z. F.; Hu, X. L. Resonance Rayleigh scattering spectra, non-linear scattering spectra of tetracainehydrochloride–erythrosin system and its analytical application. *Spectrochimica Acta Part A* **2009**, *71*, 2063–2068.
37. Yi, A. X.; Liu, Z. F.; Liu, S. P.; Hu, X. L. Study on the interaction between palladium(II)–lincomycin chelate and erythosine by absorption, fluorescence and resonance Rayleigh scattering spectra and its analytical applications. *Luminescence* **2009**, *24*, 23–29.
38. Zhang, X. L. *Coordination Chemistry*; Metallurgical Industry Press: Beijing, 1979; 240–242.
39. Zhang, L. T. *Pharmaceutical Analysis*; Central Radio TV University Press: Beijing, 2002; 253.
40. Anglister, J.; Steinberg, I. Z. Resonance Rayleigh scattering of cyanine dyes in solution. *J. Chem. Phys.* **1983**, *78*, 5358–5368.
41. Stanton, S. G.; Pecora, R.; Hudson, B. S. Resonance enhanced dynamic Rayleigh scattering. *J. Chem. Phys.* **1981**, *75*, 5615–5626.
42. Liu, S. P.; Kong, L. Interaction between isopoly-tungstic acid and berberine hydrochloride by resonance Rayleigh scattering spectrum. *Anal. Sci.* **2003**, *19*, 1055–1060.
43. Edition of Editorial Board of Chinese Macropaedia. ''*Chinese Macropaedia Biology* (II);'' Chinese Macropaedia Press: Beijing, 1991; 1374.