

REVIEW

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Spectrophotometric determination of procainamide () CrossMark hydrochloride using sodium periodate



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Abstract A simple spectrophotometric method has been described for the determination of procainamide hydrochloride. The method is based on the oxidation of procainamide hydrochloride by sodium periodate in the presence of sulfuric acid and measurement of the absorbance of the violet color formed at 531 nm. Parameters affecting the reaction were studied and conditions were optimized. Linear calibration graph was obtained from 50 to $700 \,\mu g \,m l^{-1}$ of procainamide hydrochloride and the limit of detection was $25 \,\mu g \, ml^{-1}$. The method was successfully applied for the determination of procainamide hydrochloride in pharmaceutical preparation.

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1. Introduction

Procainamide hydrochloride (1) is an antiarrhythmic reagent which is used to treat cardiac arrhythmic occurring in patients with heart disease.



Many methods have been used for the determination of procainamide hydrochloride such as gas chromatography (Ludden et al., 1978), HPLC using ion exchange resin (Shahdeo et al., 1997), reversed phase liquid chromatography (Coyle et al., 1987), thin layer chromatography (Wesley-Hadzija and Mattocks, 1977), and titrimetry using perchloric acid in the presence of mercuric acetate (Dunham, 1974).

Various spectrophotometric reagents have been used for the determination of procainamide hydrochloride. Bratton-Marshall reagent (1-naphthyl ethylene diamine) which forms colored product (Klitgaard, 1976), 4-dimethyl amino cinnamaldehyde forms a schiff base which can be measured at 542 nm was applied for the determination of procainamide hydrochloride in drugs (Tan et al., 1979), naphthoquinone 4sulfonic acid gave colored products with linearity from 50 to $250 \ \mu g \ ml^{-1}$ of procainamide hydrochloride (Gurkan, 1989), copper II ions which form a complex measurable at 380 nm (Whitaker and Hoyt, 1984), 2-amino phenol forms a red color compound with procainamide hydrochloride in the presence of potassium iodate, the method was applied to the analysis of tablets and injectable samples by measuring the absorbance at 520 nm (Sastry et al., 1985), tetracyanoquinodimethane forms a vellow product in the alkaline medium which can be measured for the determination of procainamide hydrochloride (Mohamed et al., 1991), and potassium dichromate in the presence of sulfuric acid forms a red color which can be measured at 402 nm (Al-Sharkawy, 1991).

Flow injection analysis has been used for the determination of procainamide hydrochloride using ceric sulfate (Sultan and Suliman, 1993), the reaction takes place in the presence of sulfuric acid and the absorbance of product was measured at 480 nm.

A brown product was obtained when *p*-benzoquinone was added to procainamide hydrochloride in the presence of sodium dihydrogen orthophosphate and the absorbance was measured at 501 nm (Al-Tamrah and Al-Abbad, 2004).

Periodate is one of the most important oxidizing agents, it has been used for the determination of many organic and inorganic compounds. The most important application of periodate is that of malaprade reaction (Malaprade, 1926). Various spectrophotometric methods of analysis involving periodate oxidations have been developed. The periodate oxidation of manganese II to permanganate in acidic medium followed by detection at 521 nm was used for the determination of manganese in copper-selenide (Emarkova and Podgornaya, 1989), paracetamol was determined in pharmaceutical preparation after the oxidation with periodate in sulfuric acid medium by measuring the absorbance of the yellow product at 410 nm (Al-Tamrah, 1987), Fe(III)[Fe(CN)₆] complex formed by the oxidation of Fe(II) with periodate in the presence of potassium ferrocyanide to give the intense Prussian blue color was used for its determination (Rahim and Bashir, 1984), ribavirin was determined after oxidation by periodate and measurement of the absorbance at 475 nm (Darwish et al., 2006) Periodate oxidation of methoxamine followed by photometric detection at 352 nm was used for the determination of methoxamine in drugs (Hassan et al., 2000). The periodate oxidation to phenothiazine drug followed by detection of the produced semiquinoid radicals at 500–525 nm (Basavaiah et al., 2000) and the determination of catechol amine in drugs after oxidation with periodate and coupling with *p*-toluidine and measurement of the orange product at 480 nm (Abdulrahman et al., 2005), are also another examples of periodate applications.

2. Experimental

2.1. Apparatus

All the absorbance spectral measurements were made using UV-vis spectrum Lambda 2S[Perkin-Elmer] with 10 nm quarts cell.

2.2. Reagents

All chemical reagents are of analytical grade.

a- Procainamide hydrochloride solution (Aldrich UK) $1000 \ \mu g \ ml^{-1}$ was prepared by dissolving 1 g in double distilled water with shaking for 5 min and completing the volume to 1 l with double distilled water.

b- Sulfuric acid

1 M solution of sulfuric acid (Analar BDH, 95–97%) was prepared by dissolving 27 ml in 300 ml of double distilled water and completing the volume to 500 ml with double distilled water.

c- Sodium periodate

1% solution of sodium periodate (Merck Germany) was prepared by dissolving 1 g in 100 ml of double distilling water.

d- Pronstyl, 250 mg tablets (Squibb England) was supplied from King Fahad Hospital.

When sodium periodate is added to procainamide hydrochloride, a pale yellow color is formed probably due to the oxidation of the amino group, the intensity of this color is related to the concentration of procainamide hydrochloride but cannot be used because the absorbance is very weak. The addition of sulfuric acid to procainamide hydrochloride and heating followed by sodium periodate, a violet color is obtained which can be measured at 531 nm as shown in Fig. 1.

3. Optimization of conditions

Many parameters affect the reaction and must be studied these include:

Sulphuric acid: Sulfuric acid has an important effect on the hydrolysis of procainamide hydrochloride and the formation of *p*-aminobenzoic acid. When the mixture was heated and



Figure 1 (a) The spectrum of procainamide hydrochloride against a blank of double distilled water. (b) Absorption spectrum of the product of the reaction of procainamide hydrochloride with sodium periodate in the presence of sulfuric acid against the blank (sulfuric acid and sodium periodate).

periodate was added the absorbance was found to increase with sulfuric acid concentration until 0.1 M as shown in Fig. 2.

Sodium periodate: Sodium periodate oxidizes *p*-aminobenzoic acid, the product of procainamide hydrochloride hydrolysis in the acidic medium. Different concentrations of sodium periodate from 0.001 to 0.03 M were added to a solution of $200 \ \mu g \ ml^{-1}$ procainamide hydrochloride in the presence of 0.1 M sulfuric acid. The mixture was heated at 50 °C for 5 min and the absorbance was measured at 531 nm. 0.025 M sodium periodate gave the highest absorbance as shown in Fig. 3.

Temperature: Temperature affects the reaction of periodate with procainamide hydrochloride in the presence of sulfuric acid. The effect of temperature was studied from 25 to 100 $^{\circ}$ C, the absorbance was found to increase with temperature up to 80 $^{\circ}$ C and then remains constant as illustrated in Fig. 4.

Heating time: The time needed for the reaction to complete was studied. The reagents were mixed and heated at $80 \,^{\circ}$ C from 1 to 25 min. The absorbance was found to increase with



Figure 2 Effect of sulfuric acid on the absorbance of the product.

heating time until 7 min. which was found to be enough for the reaction to complete as shown in Fig. 5.

Table 1 summarizes the optimal conditions for the reaction of periodate with procainamide hydrochloride in the presence of sulfuric acid.

4. Calibration graph

At the optimized conditions, a linear calibration graph was obtained from 50 to 700 μ g ml⁻¹ of procainamide hydrochloride with correlation coefficient of 0.999. The standard deviation was 0.027 and the limit of detection was 25 μ g ml⁻¹ as shown in Fig. 6.

5. Application

The method was applied to the determination of procainamide hydrochloride on Pronstyl tablets. Ten tablets were accurately



Figure 3 Effect of sodium periodate concentration on the absorbance.



Figure 4 Effect of temperature on the hydrolysis of procainamide hydrochloride.



Table 1 Optimal conditions for the reaction of periodate with procainamide hydrochloride in the presence of sulfuric acid.

· · ·	
Sodium periodate	0.025 M
Sulfuric acid	0.1 M
Temperature	80 °C
Heating time	7 min
λ _{max}	531 nm

weighed and an amount equivalent to 250 mg procainamide hydrochloride was dissolved in 600 ml double distilled water, the solution was heated for 5 min at 50 °C to complete dissolution. The sample was filtered and the volume was completed to 1 l with double distilled water to give a final concentration of 250 µg ml⁻¹ of procainamide hydrochloride.

One milliliter of the sample was transferred to a 10 ml volumetric flask followed by 1 ml of 1 M sulfuric acid, the sample



Figure 6 Calibration graph for procainamide hydrochloride using sodium periodate.

was heated for 7 min at 80 °C and then cooled to room temperature, 3 ml of sodium periodate (0.08 M) was added and the volume was completed to the mark with double distilled water. The absorbance was measured at 531 nm against the blank (H₂SO₄ + NaIO₄). Very good results were obtained as shown in Table 2.

6. Discussion

The hydrolysis of procainamide hydrochloride in the presence of sulfuric acid with heating has been discussed in the literature and was proved by HPLC, when the solution of procainamide hydrochloride was injected, one peak was obtained, However, in the presence of sulfuric acid, two peaks were obtained, the injections of *p*-aminobenzoic acid solution gave one peak similar to the first peak of procainamide hydrochloride acidic solution which confirms the hydrolysis of procainamide hydrochloride in acidic solution to the corresponding *p*-aminobenzoic acid (Al-Sharkawy, 1991) as shown in the equation below:

 Table 2
 Determination of procainamide hydrochloride in

 Pronstyl tablets using sodium periodate.

Sample No.	Procainamide hydrochloride ($\mu g m l^{-1}$)		
	Expected	Found	
1	25	24.98	
2	25	25.44	
3	25	25.12	
4	25	24.92	
5	25	25.01	



When sodium periodate is added it oxidizes *p*-aminobenzoic acid and violet color appears which turns quickly to brown. The same color can be obtained when periodate is added directly to *p*-aminobenzoic acid. The mechanism of the oxidation of *p*-aminobenzoic acid with periodate can be shown in the equations below:





An intermediate product is formed called nitrene, when two nitrenes combined they form azobenzene, 4-4'-dicarboxylic acid which gives the violet color (Srivastava et al., 1980).

The absorbance of the violet color formed is related to the concentration of procainamide hydrochloride and should be measured within 5 min as the color fades quickly because of the degradation of the azo compound. The method is very simple, cheap and can be applied to the analysis of procainamide hydrochloride in pharmaceutical preparations.

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