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# Colorimetric Determination of p-Benzoquinone, Hydroquinone and Paracetamol

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ABSTRACT. An accurate colorimetric method was developed for the determination of 0.5 μg/ml of p-benzoquinone, hydroquinone and paracetamol. The method is based on the reaction of p-benzoquinone with piperazine at pH 5.4. The absorbance of the complex formed is measured at 363 nm. The method was applied for the analysis of mixtures of p-benzoquinone and hydroquinone and to the determination of paracetamol in some pharmaceutical preparations. The relative standard deviation is less than 1%.

Quinones are conjugated cyclic diketones rather than aromatic compounds (Roberts and Caserio 1965). They are very important compounds and have been isolated from various biological sources such as fungi, molds and plants (Morrison and Boyd 1973). Benzoquinone and its derivatives have widely been used as analytical reagents for the determination of many organic compounds such as amines (Hassan *et al.* 1985), catecholamines (Korany *et al.* 1984), codeine, emetine and pilocarpine (Abdel-Hamid *et al.* 1985) and cations (Mahmood *et al.* 1981).

Quinones can be detected with 4-methylaminophenol (Murty and Murty 1981). They also form blue quinoidal dyestuffs if they are treated with some nitroso-compounds (Anger 1959). Different reagent sprays have been used for the detection and semiquantitative determination of p-benzoquinone (Thielmann 1974). Only very few colorimetric methods are now available for the determination of p-benzoquinone. It can be determined spectrophotometrically with 4-aminophenazone by measuring the absorbance of the red colour formed at 530 nm (Thielmann 1970). Benzoquinone can also be determined spectrophotometrically using 4-aminoantipyrine (Thielmann 1972). Benzenesulphinic acid reacts

with p-benzoquinone in acidic medium to form dihydroxyarylphenyl sulphones which can be extracted into isopropyl ether and measured spectrophotometrically at 313 nm (Stadnik *et al.* 1977), Bagdasarov *et al.* (1977) used methylamine and hydrogen peroxide for the spectrophotometric determination of p-benzoquinone. The absorbance was measured at 360 nm after 15 min.

The reaction of p-benzoquinone and amines seems to be general. It has been applied to the determination of wide range of aliphatic, primary, secondary, alicyclic and heterocyclic amines (Benson and Spillane 1976).

This work describes the development of a simple and direct colorimetric method for the determination of p-benzoquinone and the application of the method established for the analysis of other organic compounds which can produce p-benzoquinone on their oxidation.

## Experimental

A Beckman Model 35 spectrophotometer connected to a Beckman Model 24-25 ACC recorder was used for all absorbance measurements. Matched sets of W210/UU 10.00 mm cells were used throughout this work.

### *Reagents*

Quartz processed high purity distilled water was used throughout. All chemicals were of analytical grade. A stock solution of p-benzoquinone containing 1000 μg/ml was prepared by dissolving 0.25 g in about 100 ml of 95% ethanol and completing to 250 ml with distilled water. Hydroquinone solution (1000 μg/ml) was prepared by dissolving 1.0 g in distilled water and completing to one liter. Paracetamol was prepared in our laboratory by acetylation of p-aminophenol (Vogel 1958). A stock solution of 1000 μg/ml of paracetamol was prepared by dissolving 1.0 g in warm water, stirring for 10 min and diluting to one liter after cooling. Paracetamol tablets were weighed and ground into a fine powder. A mass of powder containing 500 mg of paracetamol was weighed accurately, mixed with 150 ml distilled water, warmed and stirred for 10 min. The sample was filtered through a Whatman No. 41 filter paper, washed with distilled water. The filtrate and the washing were diluted to 500 ml with distilled water.

The contents of paracetamol capsules were carefully mixed and weighed. An amount equivalent to 500 mg of paracetamol was accurately weighed and dissolved in 150 ml distilled water, warmed and stirred for 10 min. The insoluble mass was filtered through a Whatman No. 41 filter paper and washed with distilled water. The filtrate and the washings were transferred into 500 ml calibrated flask and diluted to volume after cooling to room temperature. Piperazine solution (1%)

was prepared by dissolving the appropriate amount in distilled water. The buffer solution was prepared by mixing 44.7 ml of 0.1 M citric acid and 55.3 ml of 0.2 M disodium hydrogen orthophosphate to give 100 ml of buffer solution pH = 5.4.

### *Procedure*

Transfer one ml of piperazine solution (1%) into a 50 ml standard flask. Add 2 ml of the buffer solution (pH = 5.4) and 1-5 ml of p-benzoquinone solution containing 5-50 μg/ml. Heat the mixture for 10 min at 90°C. Cool to room temperature and complete to volume with distilled water. Measure the absorbance of the orange yellow complex formed at 363 nm. For the determination of hydroquinone and paracetamol, the sample containing 5-50 μg/ml is transferred into a 50 ml volumetric flask, 5 ml of $1 \times 10^{-2}$M potassium periodate were added and the reagents were heated in a water bath at 90°C for 10 min to ensure complete oxidation. The reagents are then cooled to room temperature and the produced p-benzoquinone is determined with piperazine as above.

## Results and Discussion

p-Benzoquinone reacts quantitatively with piperazine to form a complex which has a maximal wavelength of 516 nm as shown in Fig. 1. This colour can be observed when these reagents are mixed in the alkaline medium. However, at pH

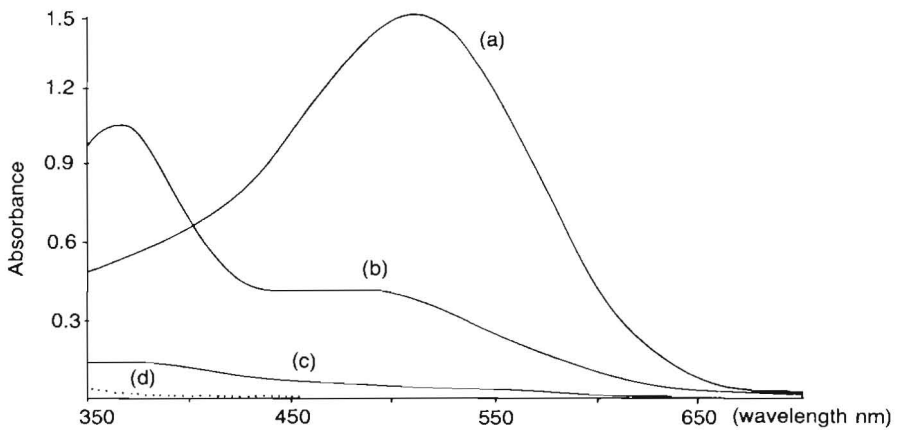
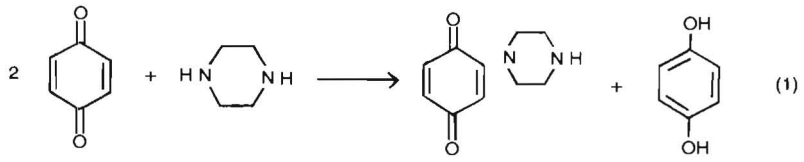
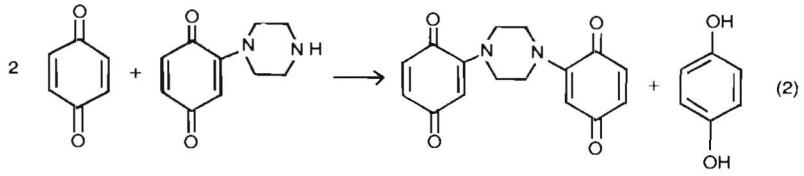



**Fig. 1.** The spectrum of p-benzoquinone-piperazine complex
a) Excess p-benzoquinone
b) Excess piperazine
c) p-benzoquinone alone
d) Piperazine alone

5.4 minimal blank reading, high stability of the complex formed and better sensitivity can be obtained. Piperazine is a good n electron donor and will form charge transfer complexes with many organic acids such as quinones. Benzoquinones are well known acceptors and hence the nature of the excitation in their interaction is an n-$\pi$ transitions. With primary amines rapid addition occurs to give the double substituted product but with secondary amines the monosubstituted product is predominant (Hikosaka 1970). In the presence of excess amounts of p-benzoquinone, a red complex is formed which has a maximal absorbance at 516 nm as shown in Fig. 1(a). However, using the continuous variations and the molar-ratio methods, the reacting ratio of p-benzoquinone to piperazine (a secondary amine) is 4:1 and not the expected 2:1, because piperazine has two nitrogen atoms capable of reacting with p-benzoquinone probably in a two-steps reaction indicating the following mechanism:

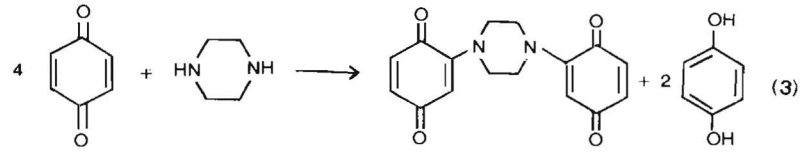


(1)



(2)

The overall reaction is



(3)

On the other hand, when piperazine is present in excess an orange yellow complex is formed which has a maximal absorbance at 363 nm, as shown in Fig. 1(b). The molar-ratio studies showed the reacting ratio of p-benzoquinone to piperazine is 2:1 as shown in equation (1). This reaction is relatively slow at room temperature and needs about 90 min. to complete, as shown in Fig. 2(a). It was

observed that if the reagents are mixed and left to react before completing to the volume, the reaction completed in about 25 min, as shown in Fig. 2(b).

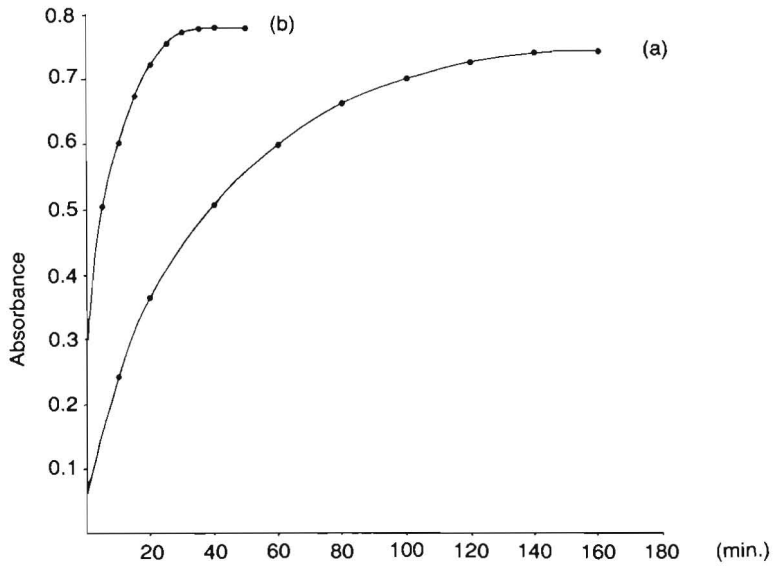



**Fig. 2.** Effect of time on the reaction of 35 μg/ml p-benzoquinone with piperazine at room temperature.
a) Reagents lift to react after dilution and (b) before dilution.

The reaction depends also on the temperature. At constant reaction time, it was found that the absorbance of the red colour formed increases significantly with increasing the reaction temperature up to 90°C. Higher temperature may cause a loss of the alcohol from the solution and must be avoided. The results obtained are shown in Fig. 3. As mentioned before, the reaction is slow at room temperature and almost less sensitive, however, at the optimal temperature established before (90°C), the reaction was found to complete within 10 minutes as illustrated in Fig. 4. Excess reagent is necessary to ensure complete reaction. 1% (w/v) piperazine was found to be suitable in the range used.

### *Calibration Graph*

At the optimal operating conditions, a calibration graph was prepared for p-benzoquinone. The absorbance of the orange complex was found to be related to the concentration of p-benzoquinone and linear calibration graph was obtained from 1-45 μg/ml of p-benzoquinone as shown in Fig. 5. The correlation coefficient is 0.998 and the relative standard deviation for 10 determinations of 25 μg/ml of p-benzoquinone is 1%. The smallest detectable amount (signal:noise is 2:1) is 0.5 μg/ml which gives a signal of 0.02 absorbance, *i.e.* twice the background noise.

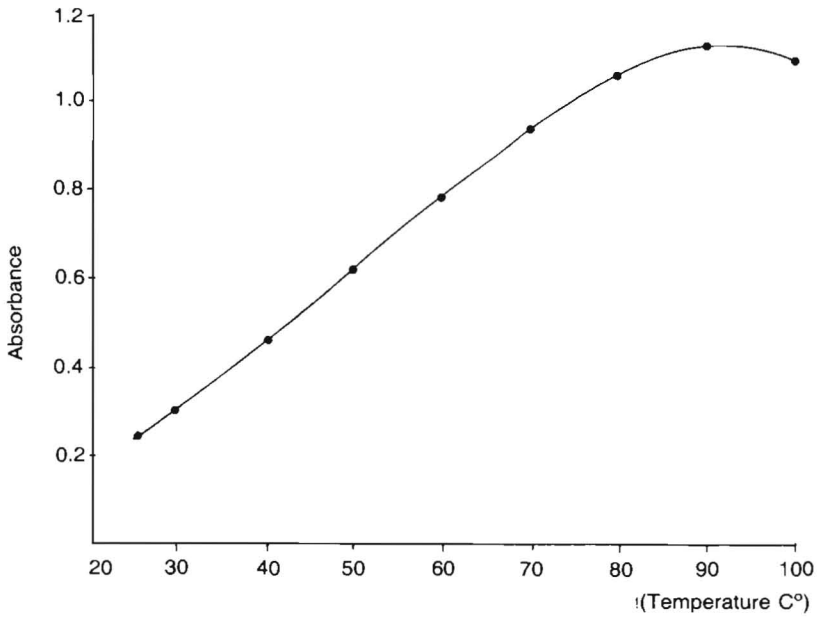



**Fig. 3.** Effect of temperature on the reaction of 35 μg/ml p-benzoquinone with piperazine

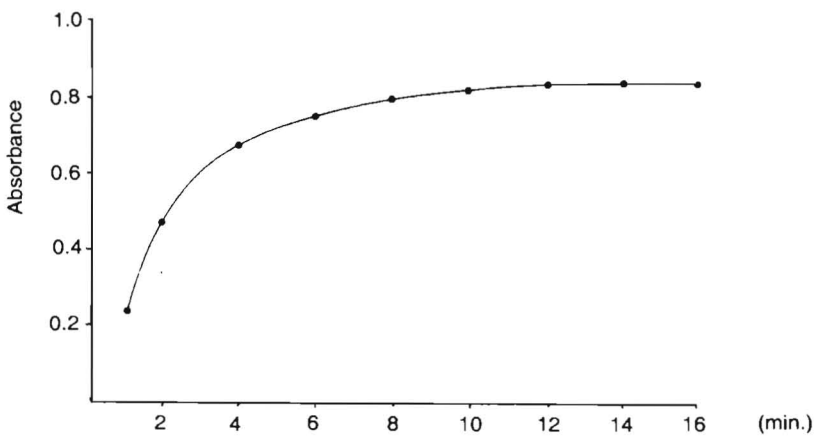



**Fig. 4.** Effect of time on the reaction of 35 μg/ml p-benzoquinone with piperazine at 90°C

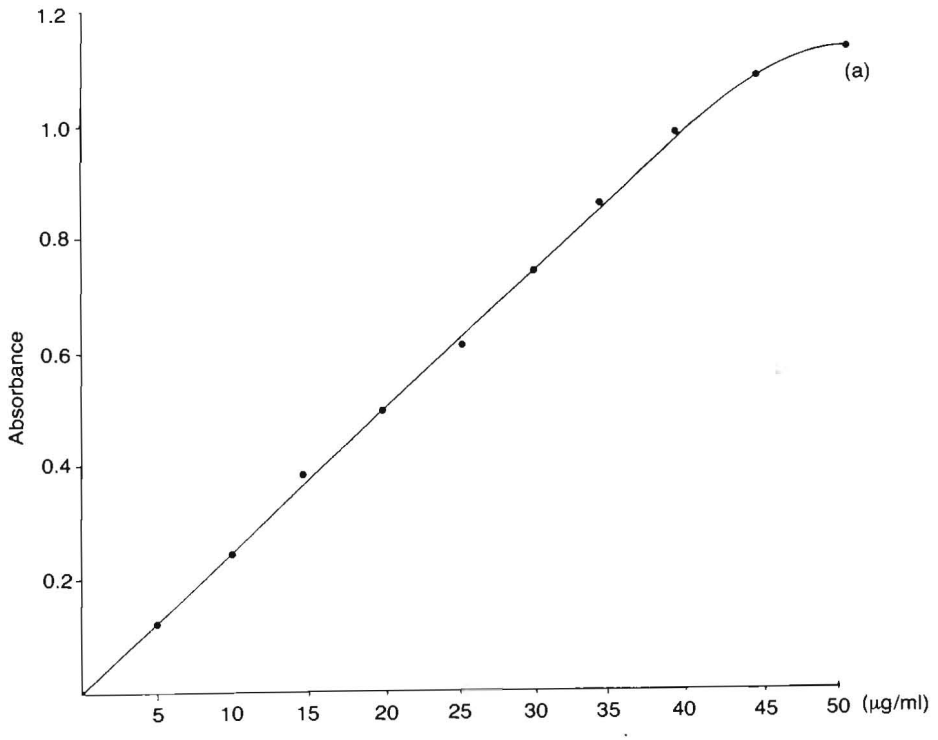



**Fig. 5.** Calibration graph for p-benzoquinone

### *Determination of Hydroquinone and Paracetamol*

Hydroquinone and paracetamol (N-acetyl-p-aminophenol) do not react with piperazine and the red colour cannot be observed when these compounds are mixed with the reagent. The weak absorbance obtained when hydroquinone is mixed with piperazine is probably due to impurities or to the air oxidation of hydroquinone to p-benzoquinone. However, in the presence of small amounts of potassium periodate, the red colour starts to appear indicating oxidation of hydroquinone and paracetamol to the corresponding p-benzoquinone which, in turns, reacts with piperazine to give the red complex. This encouraged the application of the method for the determination of hydroquinone and paracetamol. The amount of the oxidizing agent (potassium periodate) is very important and large excess of the oxidant must be avoided. The effect of potassium periodate on the oxidation of 25 μg/ml hydroquinone was investigated. $1\times10^{-3}$M was found to be suitable as summarized in Table 1.

**Table 1.** Effect of $KIO_4$ on the oxidation of 25 μg/ml hydroquinone

| Potassium periodate (M) | Absorbance |
|---|---|
| $0.5 \times 10^{-3}$ | 0.393 |
| $1.0 \times 10^{-3}$ | 0.563 |
| $1.5 \times 10^{-3}$ | 0.563 |
| $2.0 \times 10^{-3}$ | 0.564 |

Linear Calibration graphs were prepared for hydroquinone and paracetamol as shown in Fig. 6.

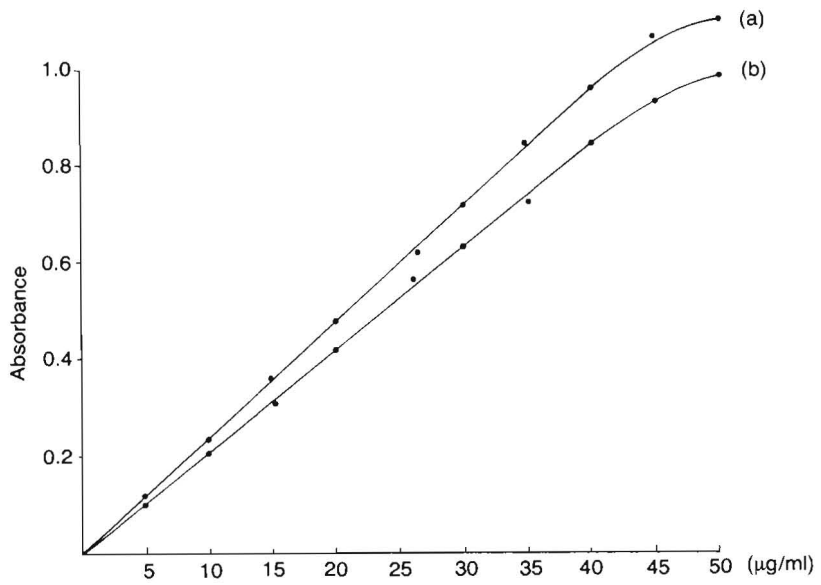



**Fig. 6.** Calibration graph for (a) Hydroquinone and (b) Paracetamol

### *Determination of p-Benzoquinone in the Presence of Hydroquinone*

Hydroquinone does not react with piperazine at the same conditions as p-benzoquinone. Therefore, a possible separation of these compounds can be achieved and it is possible to determine p-benzoquinone in the presence of hydroquinone. For total determination of p-benzoquinone and hydroquinone, potassium periodate is added before applying the piperazine method. Good

recovery was obtained when the method was applied for the analysis of mixtures of these two compounds. Hydroquinone has only very little effect on the p-benzoquinone response as shown in Table 2.

It was observed that higher concentrations of hydroquinone cause little interference in the determination of p-benzoquinone, which is probably due to the impurities or to the air oxidation of hydroquinone to p-benzoquinone as mentioned before.

**Table 2.** Determination of p-benzoquinone in the presence of hydroquinone

| p-Benzoquinone added μg/ml | p-Benzoquinone found μg/ml |
|---|---|
| 8 μg/ml p-benzoquinone + 4 μg/ml hydroquinone | 8 |
| 6 μg/ml p-benzoquinone + 4 μg/ml hydroquinone | 6 |
| 4 μg/ml p-benzoquinone + 2 μg/ml hydroquinone | 4 |
| 40 μg/ml p-benzoquinone + 60 μg/ml hydroquinone | 44 |
| 20 μg/ml p-benzoquinone + 40 μg/ml hydroquinone | 22 |

### *Determination of Paracetamol*

Paracetamol (N-acetyl-p-aminophenol) can similarly be oxidized at the same conditions to p-benzoquinone (Sultan *et al.* 1986) and can thus be determined by the same method. Analysis of authentic paracetamol samples gave good results and encouraged the application of this method to the determination of paracetamol in some pharmaceutical preparations. Results obtained are summarized in Table 3.

**Table 3.** Determination of paracetamol in Pharmaceutical preparations using piperazine

| Sample | Paracetamol* | | Recovery |
|---|---|---|---|
| | Expected μg/ml | Found μg/ml | |
| Paracetamol pure | 50.0 | 50.0 | 100.0% |
| Panadol | 50.0 | 50.0 | 100.0% |
| Revanine | 50.0 | 49.1 | 98.2% |
| Revacode | 50.0 | 49.5 | 99.0% |

* Average of three determinations

## Conclusion

The method described here for the determination of p-benzoquinone is based on the reaction of p-benzoquinone with piperazine and measuring of the absorbance of the orange colour formed at 363 nm. The method is very simple, rapid and reasonably sensitive for the determination of microgram amounts of p-benzoquinone. This encouraged the application of this method for the determination of some organic compounds which yield p-benzoquinone. Hydroquinone and paracetamol were investigated as typical examples and gave good results.

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# تقدير البنزوكينون والهيدروكينون والباراسيتامول بطريقة لونية

**سعد بن عبدالعزيز الطمره**

قسم الكيمياء ـ كلية العلوم ـ جامعة الملك سعود ـ ص. ب ٢٤٥٥ الرياض ١١٤٥١
المملكة العربية السعودية

لقد تم تطوير طريقة لونية بسيطة وذات مصداقية عالية لتقدير البنزوكينون أو الهيدروكينون أو الباراسيتامول (ن ـ استيل ـ بارا أمينوفينول). وتعتمد هذه الطريقة على تفاعل البنزوكينون مع البايبرازين في وسط حمضي عند رقم هيدروجيني يساوي ٤,٥ لتكوين معقد ملون. وقد وجد أن هذا التفاعل يعتمد على عدة عوامل منها درجة الحرارة والرقم الهيدروجيني وزمن التفاعل. وقد درست هذه العوامل بالتفصيل. فبالنسبة للحرارة وجد أنها تزيد سرعة التفاعل حيث إن التفاعل عند درجة حرارة الغرفة بطيء نسبياً وينتهي في حدود ٩٠ دقيقة، ولكن عند درجة حرارة ٩٠ درجة مئوية وجد أنه ينتهي في حدود ١٠ دقائق فقط، كذلك وجد أن الحرارة تزيد من حساسية التفاعل حيث تتناسب الحساسية تناسباً طردياً مع درجة الحرارة وعند الظروف المناسبة وجد أن امتصاص المعقد الناتج يتناسب تناسباً طردياً مع تركيز البنزوكينون. وبقياس الامتصاص عند طول موجة يساوي ٣٦٣ نانومتر أمكن تقدير كميات ضئيلة من البنزوكينون في حدود ٠,٥ ميكروجرام/مل. وقد طبقت هذه الطريقة لتقدير بعض المركبات العضوية التي يمكن أن تعطي بنزوكينون بأكسدتها، ومن أمثلتها الهيدروكينون والبارسيتامول. وقد تمت أكسدتها بوساطة فوق أيودات البوتاسيوم وبالتسخين لمدة عشر دقائق. وقد أمكن تحليل مخاليط من البنزوكينون والهيدروكينون بهذه الطريقة. كما أنها طبقت لتقدير الباراسيتامول في بعض

المستحضرات الطبية المعروفة، ومن أمثلة ذلك البنادول والـريفانـين والريفـاكود والمعـروفة بـاحتوائهـا على كميـة معلومة من البـاراسيتامـول. وقد أعـطت هذه الطريقة نتائج جيدة بالمقارنة بالطرق التحليلية المعروفة.