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# 2,3-Dichloro-5,6-Dicyano-1,4-Benzoquinone As a Redox Titrant

**A.M. El-Brash and Laila A. El-Hussain**

*Chemistry Department, Girls' College of Science, Damman 838, Kingdom of Saudi Arabia*

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An oxidimetric titrant, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in anhydrous acetic acid is used for the semimicro-determination of hydrazine hydrate, phenylhydrazine hydrochloride, isoniazid and iproniazid phosphate in pure forms as well as in some pharmaceutical preparations containing isoniazid and iproniazid phosphate. The end point was detected potentiometrically using a platinum-calomel combination electrode. The results obtained are compared statistically with those obtained by the official methods and they are in good agreement.

**Key words** : 2,4-Dichloro-5,6,dicyano-1,4-benzoquinone, Hydrazine hydrate, Phenylhydrazine hydrochloride, Isoniazid, Iproniazid, phosphate Titrimetry, Dosage forms

## INTRODUCTION

Some hydrazine compounds are studied; isoniazid is widely used for the chemotherapy of tuberculosis, iproniazid is a monoamine oxidase inhibitor and used as antidepressant (Foye, 1981). Phenylhydrazine and hydrazine are used for preparation of certain dyes, reagents for sugars, aldehydes and ketones (Kobayashi *et al.*, 1994).

As these compounds are reductants (Afkhami *et al.*, 1992; Jabbari and Shamsipur, 1993), several redox titrants have been developed for their determination. These include: *N*-bromosuccinimide (Mathur and Narang, 1974) *N*-bromophthalimide (El-Brashy and El-Ashry, 1992) potassium iodate (British Pharmacopeia, 1973), potassium bromate (British Pharmacopeia, 1993), potassium ferricyanide (Rambabu *et al.*, 1992), hydrogen peroxide (Lim and Zhong, 1989) and 2-iodoxybenzoic acid (Verma and Gultal, 1982).

In view of the interst shown in comparatively weak 1,4-benzoquinone derivatives as redox titrant the analytical possibilities of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) have been investigated using a limited number of reductants having chemical structure and significant pharmaceutical interest. It used for analysis of ascorbic acid and penicillamine (Rizk and Zakhari, 1986) and Captopril (El-Brashy, 1995).

## MATERIALS AND METHODS

### Apparatus

The end point was detected using Orion research microprocessor pH/millivolt meter 811 equipped with a platinum calomel combination electrode (13-641-578, USA).

*Correspondence to*: A.M. El-Brash, Chemistry Department, Girls' College of Science, Damman 838, Kingdom of Saudi Arabia

### Reagents

All reagents were of analytical grade. DDQ, 0.01 M solution was prepared by dissolving 2.27 g of the sample (Merk) in a litre of anhydrous acetic acid and kept in amber coloured bottles. The solution was fairly stable, its titre remains constant for more than one month. The solution was standardized iodometrically in aqueous acetous medium against 0.01 M sodium thiosulphate solution using starch as indicator.

### Materials

Isoniazid (Analar grade, BDH, Poole, Dorset, UK), Iproniazid phosphate (Hoechst-Roussel Company, London, England), are Phenylhydrazine hydrate (Fluka, AG, Germany) were purchased from the indicated compaines.

The purity of these compounds was checked by the official method which include titration with potassium bromate, in presence of potassium bromide, and potassium iodate. Solutions containing 1 $mg \cdot ml^{-1}$ and 0.005 m of these compounds were prepared in water.

### Procedure

An aliquot containing 0.5~12 mg was pipetted into a 100 ml titration cell containing a calomel platinum combination electrode. The solution was diluted with 20 ml distilled water and 5 ml orthophosphoric acid. The cell was magnitically stirred and titrated with 0.01 M DDG solution. The end point was determined graph-

ically by plotting $\Delta E/\Delta V$ against ml titrant (V).

### Procedure for tablets

Twenty tablets were pulverized and an accurately weighed amount of the powder equivalent to 25 mg of isoniazid or iproniazid phosphate was stirred with about 30 ml distilled water. The mixture was allowed to stand for 10 minutes and any residual solid was filtered and the filtrate was then quantitatively diluted to 50 ml with water in a 50 ml volumetric flask. An aliquot was taken in a 100 ml titration cell, acidified with 5 ml orthohosphoric acid and the procedure was then completed as mentioned before.

## RESULTS AND DISCUSSION

DDQ has been prepared and described as one of the most powerful organic oxidant ($E^{\circ}$=1.0 V). It is widely applied as a dehydrogenating agent (Rizk and Zakhari, 1986).

Oxidation by DDQ should be carried out in anhydrous solvents in order to avoid destructive hydrolytic displacement reaction of DDQ which are shown by dark brown colouration.

In the present investigation, the stability of DDQ solutions in anhydrous acetic acid, acetonitrile, acetone and dioxane was tested by ckeking colour and titre of standard solutions. The solution is yellow in colour and proved to be the most stable. Solutions in the other above mentioned organic solvents are less stable and daily standardization is recommended. It seems that the stability of DDQ solutions depends on the inherent acidity of the non aqueous solvent.

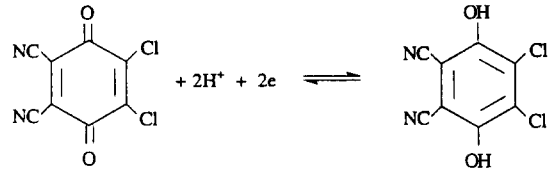
The end point was determined potentiometrically by plotting $\Delta E/\Delta V$ versus ml titrant, a steady potential was attained quickly and at the end point a potential jump was obtained.

**Table I.** Molar ratios of the reaction between hydrazine compounds and dichlorodicyanobenzoquinone

| Compound | Amt. taken, m mol. | DDQ, m mol. | Molar ratio |
|---|---|---|---|
| Hydrazine hydrate | 0.02 | 0.043 | |
| | 0.03 | 0.062 | |
| | 0.04 | 0.085 | 1:2 |
| | 0.06 | 0.117 | |
| Phenylhydrazine hydrochloride. | 0.03 | 0.062 | |
| | 0.04 | 0.081 | 1:2 |
| | 0.05 | 0.106 | |
| | 0.08 | 0.165 | |
| Iproniazid phosphate | 0.03 | 0.064 | |
| | 0.05 | 0.110 | 1:2 |
| | 0.08 | 0.175 | |
| | 0.12 | 0.236 | |
| Isoniazid | 0.04 | 0.086 | |
| | 0.06 | 0.130 | 1:2 |
| | 0.08 | 0.181 | |
| | 0.12 | 0.238 | |

Orthophosphoric acid and trichloroacetic acid were superior to many acids in that they are strong and possess no oxidizing properties.

The half-reaction of DDQ in acid medium involves 2 electrons as represented by the equation:




Dichlorodicyanobenzoquinone Dichlorodicyanohydroquinone

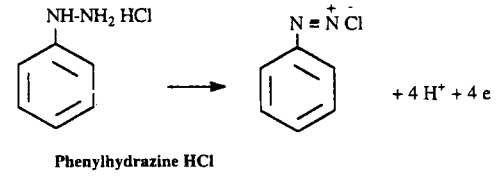
The molar ratios of the studied hydrazine compounds were found to be 1:2 as indicated in Table (I) and Fig. (1 and 2).

The stoichiometry of the oxidation reactions can be represented by the following oxidation schemes: hydrazine is oxidized to nitrogen:

$H_2N\text{-}NH_2 \longrightarrow N_2 + 4H^+ + 4e$

Hydrazine

Phenylhydrazine hydrochloride is converted to its diazonium salt:




Phenylhydrazine HCl

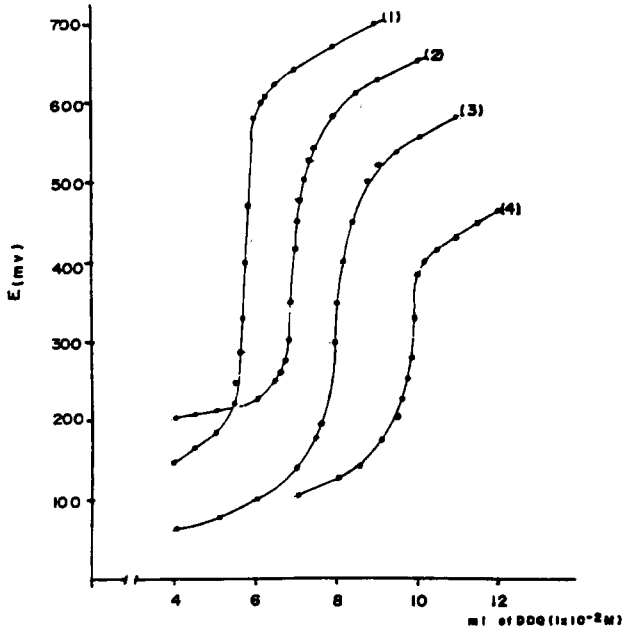



**Fig. 1.** Potentiometric titration of DDQ and: (1) Hydrazine hydrate (6 ml of $5\times10^{-3}$ M), (2) Phenyl hydrazine hydrochloride (7 ml of $5\times10^{-3}$ M), (3) Isoniazid (8 ml of $5\times10^{-3}$ M), (4) Iproniazid phosphate (10 ml of $5\times10^{-3}$ M).

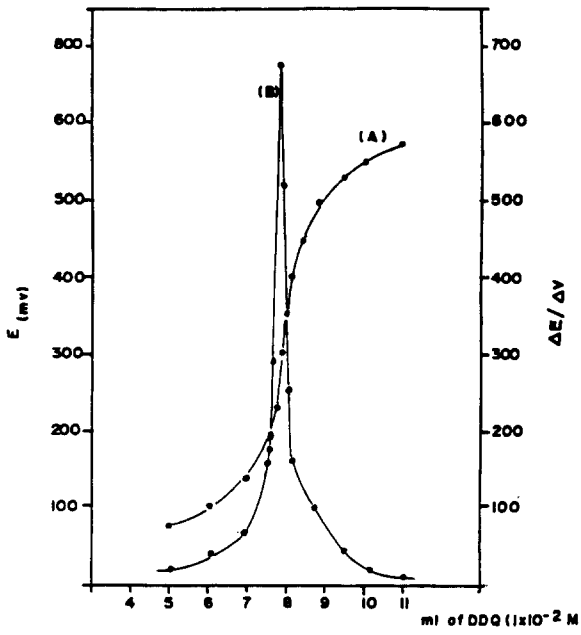
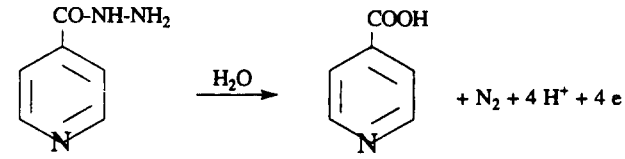


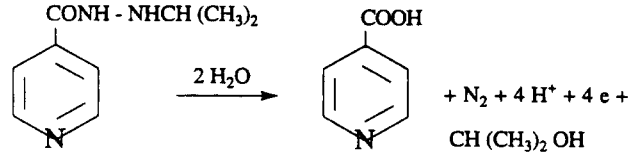

**Fig. 2.** Potentiometric titration of isoniazid (8 ml of $5\times10^{-3}$ M) with DDQ ($1\times10^{-2}$ M).

These reactions are similar to that obtained by using N-bromosuccinimide (Mathur and Narang 1974).




Isoniazid

and so, iproniazid is oxidized to isonicotinic acid and isopropyl alcohol:




Iproniazid

These reactions are similar to that obtained by using N-bromophthalimide (El-Brashy and El-Ashry, 1992), for determination of isoniazid.

The titration results are presented in Table (II) com-

**Table II.** Determination of hydrazine compounds by DDQ and official methods

| Compound | Proposed method | | Official method | |
|---|---|---|---|---|
| | Amt. taken, mg | Rec; %* | Amt. taken, mg | Rec; %* |
| Hydrazine hydrate | 0.5 | 100.61 | 100 | 100.25[7] |
| | 0.7 | 100.04 | 200 | 101.25 |
| | 1.0 | 100.00 | 300 | 100.00 |
| | 1.2 | 100.69 | 400 | 100.00 |
| | 1.5 | 101.66 | 500 | 99.50 |
| | 1.8 | 101.84 | | |
| | 2.0 | 99.38 | | |
| | 2.5 | 101.00 | | |
| Mean±C.V** | | 100.65±0.84 | | 100.20±0.65 |
| Phenylhydrazine hydrochloride. | 1.5 | 99.38 | 300 | 101.15[7] |
| | 2.0 | 100.00 | 350 | 100.86 |
| | 3.0 | 100.00 | 400 | 99.10 |
| | 3.5 | 99.00 | 450 | 100.34 |
| | 4.0 | 100.65 | 500 | 100.74 |
| | 5.0 | 100.25 | | |
| | 6.0 | 101.25 | | |
| | 7.0 | 99.00 | | |
| Mean±C.V | | 99.94±0.79 | | 100.44±0.80 |
| Iproniazid phosphate | 2.0 | 100.27 | 400 | 98.89[a] |
| | 4.0 | 99.30 | 500 | 99.83 |
| | 5.0 | 99.79 | 600 | 100.12 |
| | 7.0 | 99.00 | 700 | 98.68 |
| | 8.0 | 100.26 | 800 | 99.96 |
| | 10.0 | 99.88 | | |
| | 11.0 | 99.51 | | |
| | 12.0 | 99.67 | | |
| Mean±C.V | | 99.71±0.44 | | 99.49±0.66 |
| Isoniazid | 1.0 | 100.50 | 100 | 100.45[8] |
| | 2.0 | 101.33 | 150 | 98.81 |
| | 2.5 | 99.50 | 180 | 100.08 |
| | 3.0 | 100.99 | 200 | 99.28 |
| | 4.0 | 99.33 | 220 | 100.45 |
| | 5.0 | 101.43 | | |
| | 6.0 | 100.50 | | |
| | 7.0 | 100.00 | | |
| Mean±C.V | | 100.45±0.79 | | 99.81±0.74 |

*Average of 3 separate determinations. **Mean±coefficient of variation. (a) As isocarboxazid[6].

**Table III.** Determination of hydrazine derivatives in dosage forms by DDQ method

| Compound | Amt. taken, mg | Amt. found, mg | Rec; [%]* | Official method Rec., [%] |
|---|---|---|---|---|
| Isocid tablets[a], | 2.0 | 2.01 | 100.50 | 99.47 |
| 50 mg isoniazid/tab. | 4.0 | 3.97 | 99.33 | 101.08 |
| | 6.0 | 6.00 | 100.00 | 100.87 |
| | 8.0 | 8.01 | 100.13 | |
| Mean±C.V. | | | 99.99±0.49 | 100.47±0.87 |
| Isocid Fort, tablets[a] | 2.0 | 2.00 | 100.00 | 100.74 |
| 200 mg isoniazid/tab. | 4.0 | 4.01 | 100.25 | 99.91 |
| | 6.0 | 6.05 | 100.83 | 99.48 |
| | 8.0 | 8.03 | 100.38 | |
| Mean±C.V. | | | 100.37±0.35 | 100.04±0.64 |
| Marsilid tablets[b], | 6.0 | 5.96 | 99.40 | 100.88 |
| 25 mg | 8.0 | 7.97 | 99.63 | 100.67 |
| iproniazidphosphate/tab | 10.0 | 9.99 | 99.89 | 101.43 |
| | 12.0 | 12.01 | 100.05 | |
| Mean±C.V. | | | 99.74±0.29 | 100.99±0.39 |

*Average of 3 separate determinations.
(a) CID Company, Giza; Egypt.
(b) Hoffmann-La Roche, Basle, Switzerland.

**Table IV.** Statistical analysis of the proposed (DDQ) and official methods

| Compound | Method function | Proposed method | Official method |
|---|---|---|---|
| Hydrazine hydrate | n | 8 | 5 |
| | Rec; [%] | 100.65 | 100.20 |
| | C.V | 0.84 | 0.65 |
| | Variance | 0.71 | 0.42 |
| | F | 1.69 (6.09)* | |
| | t | 0.98 (2.20)* | |
| Phenylhydrazine hydrochloride | n | 8 | 5 |
| | Rec; [%] | 99.94 | 100.44 |
| | C.V | 0.79 | 0.80 |
| | Variance | 0.62 | 0.64 |
| | F | 1.04 (4.12) | |
| | t | 1.07 (2.20) | |
| Iproniazid phosphate | n | 8 | 5 |
| | Rec; [%] | 99.71 | 99.49 |
| | C.V | 0.44 | 0.66 |
| | Variance | 0.19 | 0.44 |
| | F | 2.31 (4.12) | |
| | t | 0.70 (2.20) | |
| Isoniazid | n | 8 | 5 |
| | Rec; [%] | 100.45 | 99.81 |
| | C.V | 0.79 | 0.74 |
| | Variance | 0.62 | 0.55 |
| | F | 1.13 (6.09)* | |
| | t | 1.45 (2.20)* | |

n: Number of experiments.
C.V: Coefficient of variation.
F: Variance ratio.
t: Student's-t-test.
*The Values between barckets are the tabulated ones at P= 0.05[166]

pared with those of official methods (British Pharmacopeia 1973, 1993).

The proposed procedure has been applied to the determination of isoniazid and iproniazid phosphate in their tablets and the results are given in Table (III). Commonly used excipients, diluents and lubricants such as lactose, starch, magnesium stearate and talc do not interfere with the determination.

There is no significant differences between the results obtained by the proposed and official methods as indicated from calculating the student's-t-values and variance ratios (Table IV) (Morris and Rolph, 1981).

The proposed method has the advantage over the official procedures of being a semimicro-determination which is also applicable to dosage forms.

## REFERENCES CITED

Afkhami, A., Safavi, A. and Massoumi, A., Spectrophotometric determination of trace amounts of selenium with catalytic reduction of bromate by hydrazine in hydrochloric acid media. Talanta, 39, 993-996 (1992).

British Pharmacopeia, Her Majesty's Stationary Office, London, 1973.

British Pharmacopeia, Her Majesty's Stationary Office, London, 1993.

El-Brashy, A. M. and El-Ashry, S. M. Colorimetric and Titimetric assay of isoniazid. *J. Pharm. Biomed. Anal.* 10, 421-426 (1992).

El-Brashy, A. M. Titrimetric determination of Captopril in dosage forms. *Acta Pharm. Hung.* 65, 91-93 (1995).

Foye, W. Q. Principles of medicinal chemistry, Lea & Fabiger, Philadelphia, 1981.

Jabbari, A. and Shamsipur, M. Spectrophotometric determination of trace amounts of molybdenum (VI) based on catalytic reduction of safranin by hydra-

zine dihydrochloride. J. Fresenius' *J. Anal. Chem.* 347, 26-271 (1993).

Kobayashi, K., Yoshimoto, K., Hirauchi, K. and Uchida, K. Determination of glycated proteins in biological sample based on colorimetry of 2 Keto-glucose released with hydrazine. *Biol. Pharm. Bull.* 17, 365-369 (1994).

Lim, P. K. and Zhong, Y. The copper-catalyzed redox reaction between aqueous hydrogen peroxide and hydrazine. *J. Am Chem. Soc.* III, 8404-8410 (1989).

Mathur, N. K. and Narang, C. K. Determination of orgainc compounds with N-bromosuccinimide and allied reagents. Academic Press London, 1974.

Morris, C. N. and Rolph, J. E. Introduction to Data analysis and statistical inference, Prentice-Hall, London, 1981.

Puri, J. K., Vats, V. K. and Sharma, V. Oxidation reduction reactions and analysis of thioureas, hydrazines and ascorbic acid in fused monobromoacetic acid. *Indian J. Chem.* 25, 565-570 (1986).

Rambabu, C., Rao, K. and Rao, K. S. Hexacyanoferrate (III) as an oxidant for the titrimetric determination of benzoyl hydrazines. *Asian J. Chem.* 4, 384-386 (1992).

Rizk. M. S. and Zakhari, N. A. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone as a redox titrant. IL Farmaco-Ed. Pr. 41, 75-82 (1986).

Verma, K. K. and Gultal, A. K. Determination of isoniazid in drugs with 2-iodoxybenzoate. *Anal.* Chem. 54, 2550-2552 (1982).