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# A novel method for spectrophotometric determination of isopropamide iodide in pharmaceutical formulations Application to content uniformity testing

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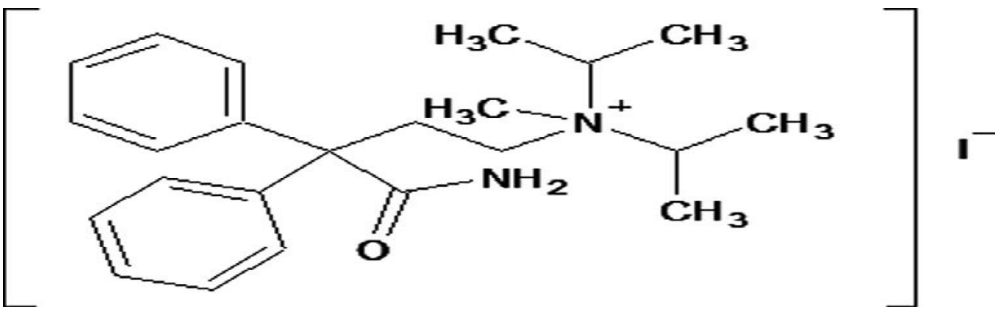
## Abstract

A simple, accurate, economical, and rapid spectrophotometric method for the determination of isopropamide iodide in pharmaceutical preparation (tablets) has been developed. The method is based on the reaction of isopropamide iodide and sodium nitrite in sulfuric acid medium to form iodine which shows maximum absorbance at 449 nm. Beer's law was obeyed in the concentration range ( 20-240µg/ml). The molar absorptivity and Sandell's sensitivity of the colored complex are $0.67\times10^3$ l/mol.cm. and 0.717 ng/cm$^2$ respectively .The limits of detection and quantization are 5.8 and 17.4 µg/ml respectively. The analytical parameters were optimized and the method was successfully applied to the determination of isopropamide iodide in pure form and its tablets form.

**Key words: Isopropamide iodide, spectrophotometry, sodium nitrite**.

## Introduction

Isopropamide iodide, (3-carbamoyl-3,3- diphenylpropyl) di- isopropylmethyl ammonium iodide (Figure .1), is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine. It is used as an adjunct in the treatment of peptic ulcer disease, in the relief of gastrointestinal and urinary-tract disorders associated with smooth muscle spasm [1]..




Molecular formula: C23H33IN2O

Molecular weight: 480.42

**Figure (1): Chemical structure of isopropamide iodide.**

The literature survey reveals that several methods have been reported for determination of isopropamide iodide in pure form and in pharmaceutiacal formulations. Official method includes non aqueous titration with perchloric acid for pure form and Uv spectrophotometric method for tablets [2]. The spectrophotometric method include second derivative and ion-pair complexation reaction [3-8].Other methods reported for determination of isopropamide iodide like high-performance liquid chromatography[ 9-12], Spectrophotometry is by far the instrumental technique of choice in the laboratories of underdeveloped and developing nations for the quantification of drugs, owing mainly to its simplicity, high sensitivity & selectivity and often demanding low-cost equipment. The objective of the present work is to develop and validate a simple, accurate and economically viable spectrophotometric method for the determination of isopropamide iodide in bulk and in their pharmaceutical formulations. The proposed method was based on the reaction of isopropamide iodide with sodium nitrite in acetic acid medium to form iodine which quantities spectrophotometrically at 449 nm. The proposed method was successfully applied to the determination of isopropamide iodide in pure form and its tablets form.

## Experimental

### Apparatus

Shimadzu UV- 1700 pharmaspec (double beam) spectrophotometer with 1.0 cm quartz cells was used for absorption measurements.

### Reagents

All chemical used were of analytical or pharmaceutical grade and distilled water was used throughout. Standard materials and pharmaceutical preparations (isopropamide iodide tablets) were provided from ALhokamaa Company for pharmaceutical industries (HPI) Mosul-Iraq.

**Isopropamide iodide solution (0 .1%):** This solution was prepared by dissolving 0.1 gm of isopropamide iodide in 100 ml distilled water in a volumetric flask

**Sodium nitrite solution** (1%).This solution was prepared by dissolving 1 g of sodium nitrite in 100 ml of distilled water.

**Sulfuric acid 1N:** This solution was prepared by diluting 2.78 ml of (36 N Sulfuric acid) to 100ml by distilled water in a volumetric flask.

## Recommended procedure

Aliquots of standard drug solution of isopropamide iodide 0.5- 6 ml were taken and transferred into a series of 25 ml of volumetric flask. To each flask 3.0 of 1N $H_2SO_4$ and 1ml of sodium nitrite was added. The volume was made up to the mark with distilled water and the absorbance was measured at 449 nm against reagent blank.

**Procedure for pharmaceutical preparations (tablets)**

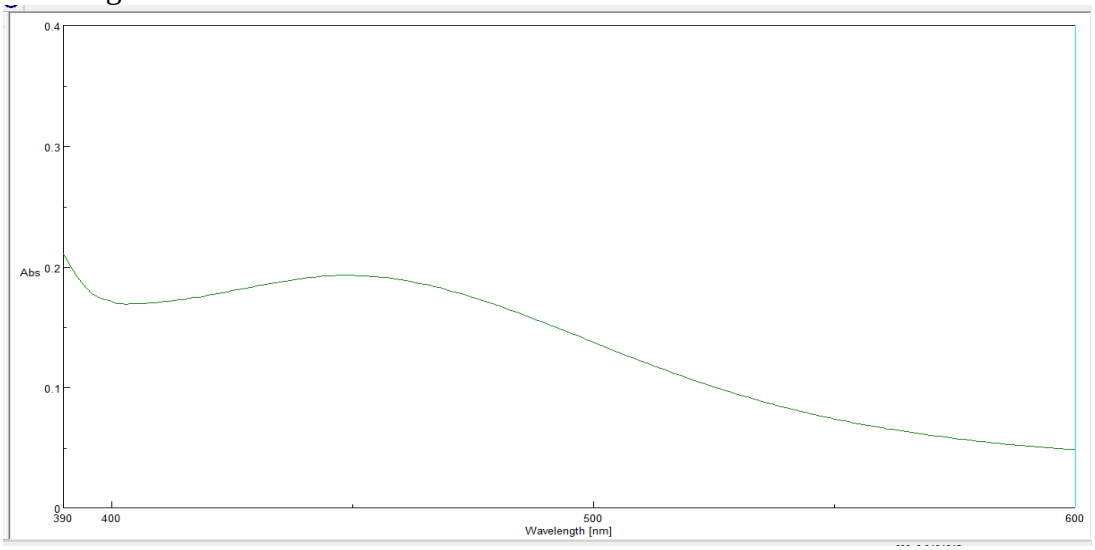
To minimize a possible variation in the composition of the tablets, the mixed content of 20 tablets, were weighed and grounded, then the powder equivalent to 100 mg of isopropamide iodide was stirred well with 50 ml of water for 20 mints. and then filtered through whatman No. 42 filter paper and the volume was made to 100 ml with distilled water. Treat 3ml of this solution as mentioned under recommended procedure.

## Results and Discussion

The method involves the liberation of iodine by the reaction of isopropamide iodide and sodium nitrite in 1N $H_2SO_4$ medium to form iodine [13].

$$2NaNO2 + H_2SO_4 \rightarrow 2HNO_2 + NaSO_4$$
$$2HNO_2 + 2I \rightarrow I_2 + 2NO + 2H_2O$$

The absorption spectra of the product against blank were recorded. The colored product showed maximum absorption at 449 nm as shown below (Figure. 2) and this wavelength was recommended for determination.




**Figure[2]: Absorption spectra of A: 120µg /ml of isopropamide iodide against reagent blank.**

**Study of the optimum reaction conditions**

The effect of various parameters on the absorption of the product formed was studied and the reaction conditions are optimized.

**Effect of acid**

The effect of different acids on the absorbance of the colored product shows that maximum intensity was reached when using 3 ml of 1 N sulfuric acid solution. This amount was selected for the subsequent experiments.

**Effect of sodium nitrite reagent**

The effect of the amount of NaNO2 solution on the absorbance of the colored product was studied. It was observed that the addition of 1 ml of 1 % NaNO2 solution was required to obtain a maximum absorbance. This amount was selected for subsequent experiments.

**Effect of temperature and time:**

The results obtained indicated that complete color formation occurred immediately and not effected by temperature. Higher temperature causes turbid color; therefore, room temperature was selected as suitable temperature. The absorbance remained constant for 6 hours at least, and 5 min was selected as a suitable time.

**Effect of order of addition**

To obtain optimum results the order of addition of reagent should be followed as given under the recommended procedure.

## Calibration graph

Under the experimental conditions described, Beer's law is obeyed over the concentration range 20-240µg/ml (Figure.3). Linear regression equation: Y=0.0014x+0.0247, ($R^2$ = 0.998, n =7). Where Y is the absorbance and X is the concentration in µg\ml The apparent molar absorptivity was $0.67\times10^3$ $L.mol^{-1}.cm^{-1}$ and Sandell's sensitivity was 0.717ng/$cm^2$ The limit of detection (LOD) and limit of

quantification(LOQ) were calculated as the ratio of 3.3 and 10 standard deviation of the blank (n=7) respectively, and the slope of the calibration line [14].The limit of detection was 5.8µg/ml and the limit of quantification as the lowest standard concentration which could be determined with acceptable accuracy, and precision was 17.4µg/ml

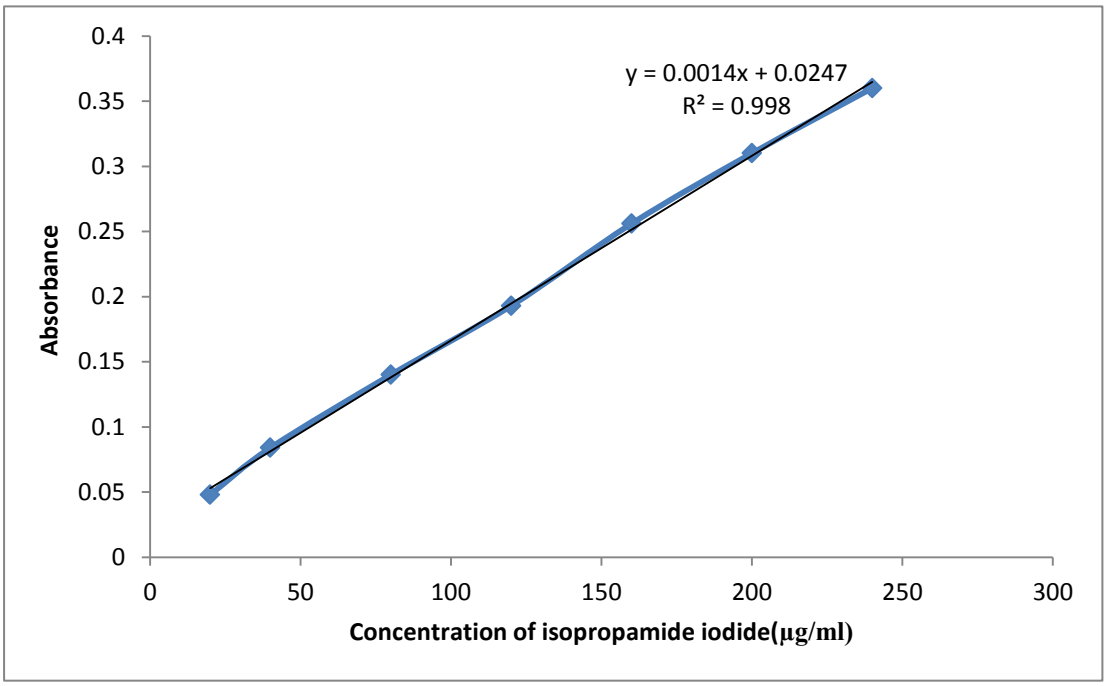



**Figure [3]: Calibration graph of isopropamide iodide.**

## Accuracy and precision:

The accuracy and precision of the method were established by analyzing the pure drug solution at three different levels. The average recovery which is a measure of accuracy is 100 ±0.89% revealing high accuracy of the method. The relative standard deviation (RSD), which is an indicator of precision, is less than 1.5%, the result are complied in Table.1

**Table [1]: Optical characteristics and statistical data for regression equation of the proposed method**

| Parameters | Value |
|---|---|
| λ max (nm) | 449 |
| Beer´s law limits (µg .ml$^{-1}$) | 20-240 |
| Molar absorpitivity (1.mol$^{-1}$.cm$^{-1}$) | 0.67× 10$^{3}$ |
| Sandell s Sensitivity(ng/cm$^{2}$) | 0.717 |
| Correlation coefficient ($r^2$ ) | 0.998 |
| Regression equation (Y= a × + b ) | |
| Slope (a) | 0.0014 |
| Intercept (b) | 0.0247 |
| Recovery % | 100 ± 0.89 |
| Relative standard deviation (%) | < 1.5 |

## Interferences Study

In order to assess the possible of the proposed method, the effect of substance that often accompany with isopropamide iodide in pharmaceutical product(Tablets) were studied by adding different amount of substances to 120µg/ml of isopropamide

iodide. An attractive feature of the method is its relative freedom from inference by the usual diluents and excipients in amount for in excess of their normal occurrence in pharmaceutical preparations. The results are given in Table 2.

**Table[2]: Determination of 120 µg/ml of isopropamide iodide in the presence of excipients and other substances.**

| Interfering substances | Amount added(mg) | Amount of isopropamide iodide found(µg) * | RSD % |
|---|---|---|---|
| Benzyl alcohol | 1 | 120.99 | 0.88 |
| Chlorobutanol | 10 | ١21 | 0.91 |
| Lactose | 40 | 120.8 | 0.71 |
| Microcrystalline cellulose | 20 | 120.6 | 0.64 |
| Magnesium stearate | 40 | ١٢١ | 0.91 |
| Hydroxyl propyl methyl cellulose | 40 | ١٢١ | 0.93 |

*Average of six determinations.

## Analytical application:

The proposed method was satisfactorily applied to the determination of isopropamide iodide in its pharmaceutical preparations tablets , the results revels that there is close agreement between the results obtained by the proposed method and the label claim Table 3.

**Table[3]: Determination of isopropamide iodide in pharmaceutical formulations**

| Pharmaceutical formulations | Label amount( mg) | Found by proposed method *mg | Recovery% |
|---|---|---|---|
| Tablets | 5mg/tab | 4.96 | 99.8 |

*mean value of ten determinations

## Application of the proposed method to content uniformity [2, 15]

Content uniformity or the uniformity of dosage unit was defined as the degree of uniformity in the amount of active substance among dosage units. The risk assessment strategy underlying content uniformity testing is the assumption that some pre-specified limits exist where safety and efficacy outcomes may change if content uniformity fails. The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in Table.4 indicate that the proposed method can accurately and precisely quantities of isopropamide iodide in its commercially available tablets. The mean percentage with (RSD) of the labeled claim found in ten tablets was (0.822%) which falls within the content uniformity limits specified by the by the United State Pharmacopeia 33-NF28USP 33 [2].

**Table [4]: Content uniformity testing of isopropamide iodide tablets**

| Parameter | % of the label claim |
|---|---|
| Sample.1 | 101.2 |
| Sample.2 | 99.58 |
| Sample.3 | 101.2 |
| Sample.4 | 100.2 |
| Sample.5 | 99.8 |
| Sample.6 | 100.5 |
| Sample.7 | 99.8 |
| Sample.8 | 101.8 |
| Sample.9 | 101.5 |
| Sample.10 | 99.5 |
| Mean(X) | 100.508 |
| %RSD | 0.822 |
| Max. allowed unit value[2] | ±15% |

## Conclusion

The developed method is found to be accurate, simple, precise and economical, the method free from such experimental variables as heating or solvent extraction step. The method relies on the use of simple and cheap chemicals and techniques and can be used for rapid routine determination and quality control analysis of isopropamide iodide in pure form, bulk, and pharmaceutical formulations samples.

## Acknowledgments

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# طريقة طيفية مبتكرة لتقدير الايزو بروب امايد ايوداید في مستحضراته الدوائية وتطبيق الطريقة لفحص الاتساق


## الخلاصة

تم اختبار طريقة طيفية جديدة مباشرة لتقدير الايزو بروب امايد ايوداید في حالته النقية وفي بعض مستحضراته الدوائية (الحبوب) ،تتميز الطريقة بالبساطة والانتقائية والدقة وتعتمد الطريقة على تفاعل الايزو بروب امايد ايوداید مع نتريت الصوديوم في وسط حامض الكبريتيك لتحرير اليود واللذي له اقصى امتصاص عند ٤٤٩ نانومتر حيث امكن تطبيق قانون بير على التراكيز ٢٠-٢٤٠ مايكوغرام لكل مل وبامتصاصية مولارية٠.٦٧ $\times$ ١٠$^{٣}$ لتر.مول$^{-١}$.سم$^{-١}$ وبدلالة ساندل (دلالة الحساسية) ٠.٧١٧ نانوغرام\سم$^{٢}$ وان حد الكشف والحد الكمي كانا 5.8 و ١٧.4 نانوغرام\مل على التوالي. وطبقت الطريقة بنجاح لتقدير لتقدير الايزو بروب امايد ايوداید في حالته النقية وفي بعض مستحضراته الدوائية (الحبوب)