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# Spectrophotometric method for the determination of benzocaine by cerium ammonium sulphate with promethazine hydrochloride in pure and pharmaceuticals preparation

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ABSTRACT

Easy, the accurate, sensitive spectrophotometric method used to determine Benzocaine in a pure and pharmaceutical preparation. The proposed method depends on using Promethazine hydrochloride as a reagent. Where it depends on oxidative coupling reaction of benzocaine by cerium ammonium sulphate with promethazine hydrochloride in the presence of hydrochloric acid to form green dye product, λmax 615 nm. Beers law is obeyed in the concentration of (5 –300 µg.ml$^{-1}$). The molar absorptivity is (1.77 * 10 $^{3}$) L.mol $^{-1}$.cm$^{-1}$, a sandal sensitivity of (0.0098) µq.cm$^{-2}$ and RSD (± 0.56 %). The method gave a successful determination for benzocaine in a pharmaceutical preparation.

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## INTRODUCTION

Benzocaine is a 4-aminobenzeneethyl ester, a local anaesthetic of the low type of water, and is used as a local anaesthetic for sheep, cows, horses and pigs for an extended period. Benzocaine is a local anaesthetic that temporarily inhibits nerve impulses by influencing the permeability of sodium ions through Wall of neurons (The European Agency, 1997). Another important use of benzocaine is the sedative and soothing of fish and some amphibians such as frogs the addition of 25 mg of benzocaine / L to a fish pond will cause a decrease in ammonia and kabon dioxide. As a result of this effect, it will significantly reduce the effectiveness of the fish and maintain a constant water pH. When not added by benzocaine, ammonia and carbon dioxide will dilute the water which negatively affects fish (J.T.Ferrira, *et al.,* 1984). Other important uses of benzocaine are to be analytically used in estimating many important compounds. Benzocaine was used in the evaluation of some phenolic antibiotics such as cefadroxil, amoxicillin, vancomycin (S.M.El-Ashiry, *et al.,* 2000). In addition, benzocaine is used in the estimation of nylidrin hydrochloride, isoxsuprine hydrochloride, as well as salbutamol sulphate, where these compounds interact with the benzocaine oxidised in the middle of trimethylamine to form an orange-coloured pigment (R.T.Sane, *et al.,* 1985). Literature survey indicated that few analytical methods had been reported for analysis benzocaine. They include some spectrophotometric method (F.Belal, S *et al.,* 2003; N.S.Othman 2001; R.A.A.Zakaria 2004; N.D.Dinesh, *et al.,* 2002; M.Q.Al-Abachi, *et al.,* 1990), flow injection analysis (K.K.Verma, and K.K.Strwart 1988; Al-Grawi, E.D.C., and G.R.L. Al-Awsi. 2018). In the present study, we succeeded in developing coupling agent for sensitive and selective spectrophotometric determination of the benzocaine drug based on the oxidative drug by cerium ammonium sulphate in Acidic medium which reacts with promethazine hydrochloride, to the formation of coloured products complex.

## MATERIALS AND METHODS

UV-Visible spectrophotometer Cintra-GBC Scientific Equipment, Spectrophotometric CECIL-CE 1021 and 1 cm matched quartz cells was used for absorption measurements, WTW 720 PH meter, Electronic balance (Sartorius AG Germany).

### Reagents

Benzocaine Solution (100 µg.ml$^{-1}$), prepared by dissolving (0.01 gm.) Benzocaine in (5 ml) ethanol and then diluted with distilled water to 100 ml. Cerium ammonium sulphate solution (100 µg.ml-1), prepared by dissolving (0.2gm) in distilled water and diluting to mark in 100 ml volumetric flask. Promethazine hydrochloride solution (100 µg.ml-1), prepared by dissolving (0.2gm) in distilled water and diluting to mark in 100 ml. Hydrochloric acid solution (11.8M), prepared by taking (0.8 ml) from solution concentration and diluting distilled water to mark in 100 ml.

### Procedure for assay of Benzocaine in pharmaceutical preparations

Lozenges of benzocaine solution (100 Mg.ml), prepared by dissolving (100 mg) of benzocaine and (5 mg) Borax with (0.4 mg) of menthol and diluting of solution concentration in (2 ml) of ethanol and diluting distilled water to mark in 100 ml. Throat Lozenges (100Mg.ml), prepared by dissolving (5mg) of benzocaine and (3mg) of cyriel chloride Bredin and diluting solution concentration in (2ml) of ethanol and diluting distilled water to mark in 100 ml.

**Procedures:** Into a series of 25 ml volumetric flask, transfer an increasing volume of Benzocaine solution (100 µg.ml$^{-1}$) to cover the range of calibration curve (5 – 300) µg.ml$^{-1}$, added (3 ml) cerium ammonium sulphate (100µg.ml$^{-1}$) and shake well. Added (3 ml) promethazine hydrochloride (100 µg.ml$^{-1}$). Added (4 ml) of HCL, diluted to the mark with distilled water, and stand for 30 min at (25 Ċ). Measure the absorption at (615) nm against the blank prepared in the same method but no Benzocaine.

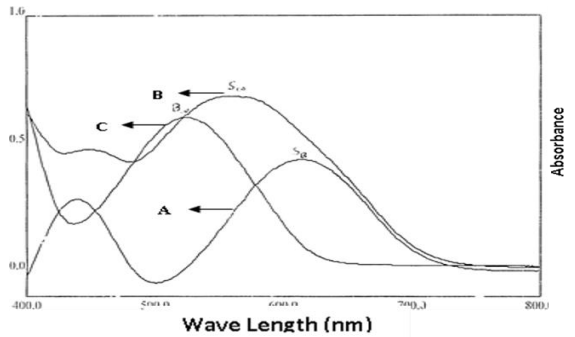


**Figure 1: :( A) Sample solution (100mg / 25ml) Vs. Blank. (B): Sample solution vs distilled water. (C): Blank Vs. distilled water**

## RESULTS AND DISCUSSION

Benzocaine drug reacts with cerium ammonium Sulphate and promethazine in the presence of Hydrochloric acid as acidic media to form an intense green colour product that can be measured spectrophotometrically at 615nm Figure (1).

### Optimisation of the reaction conditions

**Effect of cerium ammonium Sulphate volume:** The best conc. Of cerium sulphate solution was found to be 3 ml cerium ammonium sulphate (100 µg.ml$^{-1}$) for Benzocaine. Figure 2.

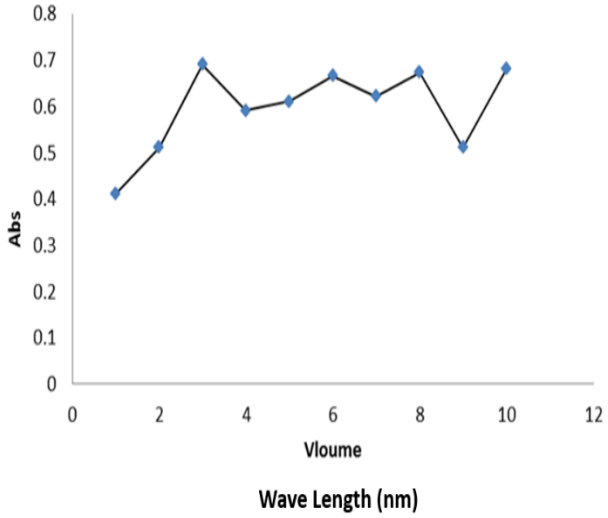


**Figure 2: Effect of cerium ammonium sulphate volume**

### Coupling agent

The effect of varying the concentration of coupling reagent was studied using the proposed procedure and adding 1 – 10 ml 0f (100 µg.ml$^{-1}$) of promethazine hydrochloride. It was found that maximum and stable Colors were formed with 3 ml of promethazine hydrochloride solution for Benzocaine in a final volume of 25 ml. Figure 3.

### Degree of temperature

The different temperature on oxidative coupling was studied for Benzocaine it was found the best temperature at room temperature (25°c). Figure 4.

**Hydrochloric acid volume:** Optimum concentration hydrochloric acid was found to be 4 ml of hydrochloric acid.

**Effect of order of addition:** Table (1), shows the order of addition could be followed, (Drug: cerium ammonium sulphate: promethazine hydrochloride: hydrochloric acid). Due to show the highest absorption and thus was selected for further use.

**Table 1: Effect of order of addiction**

| Order of addition | Abs. 615 nm | No. |
|---|---|---|
| Drug: cerium ammonium sulphate: promethazine hydrochloride: hydrochloric acid | 0.472 | 1 |
| Drug: hydrochloric acid: cerium ammonium sulphate: promethazine hydrochloride | 0.323 | 2 |
| Drug: promethazine hydrochloride: cerium ammonium sulphate: hydrochloric acid | 0.441 | 3 |
| Drug: cerium ammonium sulphate: hydrochloric acid: promethazine hydrochloride | 0.412 | 4 |
| hydrochloric acid: Drug: cerium ammonium sulphate: promethazine hydrochloride | 0.442 | 5 |

**Table 2: Result application of pharmaceutical for benzocaine**

| Mg of benzocaine | Absorbance | Lozenges of benzocaine | | Throat Lozenges | |
|---|---|---|---|---|---|
| | | A | Recovery % | A | Recovery % |
| 10 | 0.055 | 0.052 | 97.07 | 0.053 | 103.7 |
| 25 | 0.129 | 0.116 | 96.32 | 0.117 | 98.47 |
| 50 | 0.233 | 0.224 | 100.8 | 0.225 | 100.6 |
| 100 | 0.441 | 0.447 | 99.22 | 0.451 | 99.89 |

**Table 3: comparison of the method**

| Analytical parameters | Present method | Literature method* |
|---|---|---|
| pH | Acid medium | Acid medium |
| Temperature $C^0$ | At room temperature | At room temperature |
| $\lambda_{max}$ (nm.) | 615 | 525 |
| Medium of reaction | Aqueous | Aqueous |
| Reagent | Promethazine | p-benzoquinone |
| Molar absorptivity (l.mole-1.cm-1) | $1.77x10^3$ | $1.6x10^3$ |
| Colour of the dye | Green | Red |
| Sandell sensitivity(µg.$cm^{-2}$) | 0.0098 | 0.097 |
| Nature of the dye | 1: 2 | 1: 1 |
| Application method | Determination benzocaine in two drugs | Determination benzocaine in two drugs |

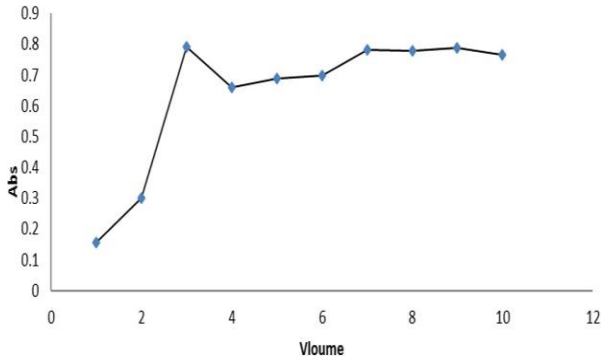


**Figure 3: Effect of coupling agent**

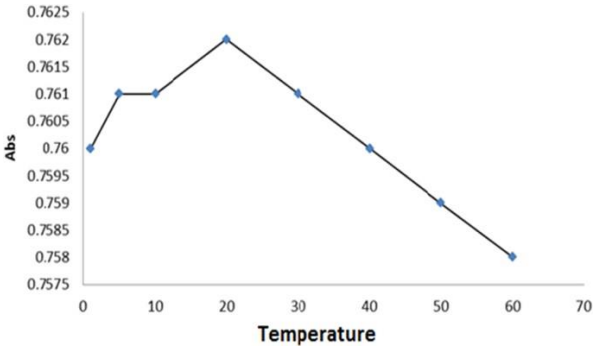


**Figure 4: Effect of temperature**

**Calibration Curve:** Using optimum condition, a linear calibration curve for the determination Benzocaine was determined over the concentration range of (5– 300) µg.$ml^{-1}$. The linear regression equation for the determination Benzocaine is (Y= 0.0042x + 0.0165) and correlation coefficient of 0.99974, the linear calibration curve Figure (5).

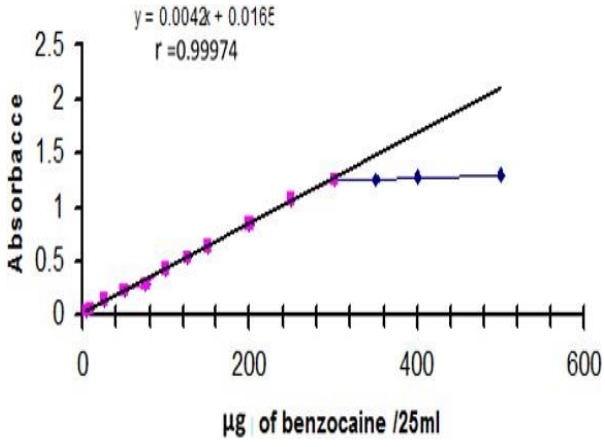


**Figure 5: The linear calibration curve**

**Nature of the dye product**

The stoichiometry of the reaction between Benzocaine, cerium ammonium sulphate, promethazine hydrochloride and hydrochloric acid was investigated using the mole ratio using the optimised conditions, the results in Figure (6).

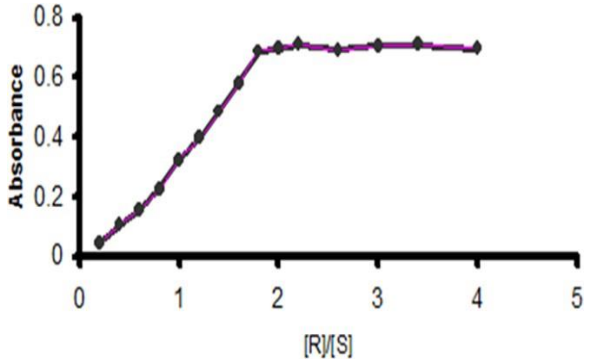


**Figure 6: the Molar ratio of drug to the reagent**

**Pharmaceutical applications**

The proposed method has been applied for the determination of Benzocaine drug in pharmaceutical preparations with good accuracy for the drugs studied. The results obtained were given in Table (2).

**CONCLUSION**

An easy, accurate and excellent spectrophotometric method was investigated for the determination of Benzocaine in pure and in pharmaceutical preparations. The proposed method can be carried out with no need for further steps such as solvent extraction step. PH. or temperature control.

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