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*Short Communication*

# Titrimetric determination of *para*-aminobenzoic acid using *N*-bromophthalimide and *N*-bromosaccharin

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**Keywords**: *Titrimetric analysis; p-aminobenzoic acid; N-bromophthalimide; N-bromosaccharin.*

*Para*-aminobenzoic acid (PABA) is extensively used in pharmaceutical and cosmetic preparations against sunburn and UV radiation effects. It is effective in preventing light-induced skin cancer and premature ageing of the skin [1]. In view of the importance of PABA in modern life, its analysis is of great significance. The analytical methods that have been used for assay, include nitrate titration [2], alkalimetry [3], bromometry using a variety of brominating agents [4–6] and colorimetry [7]. Taking into consideration the use of *N*-bromophthalimide (NBP) and *N*-bromosaccharin (NBSA) as better brominating agents in titrimetric methods [8–12] we thought it would be interesting to try to develop some better titrimetric methods for the analysis of PABA and some of its pharmaceutical preparations. Our attempt has had promising results which are reported here.

## Experimental

### *Apparatus*

A Toshiniwal titration potentiometer (type CLO 6A) fitted with a "null meter" detector, magnetic stirrer and a platinum/SCE electrode assembly was used for direct potentiometric titrations using NBSA.

### *Reagents*

Both NBP and NBSA were prepared by brominating phthalimide and saccharin, respectively, and their standard solutions (~0.01 M) in anhydrous acetic acid were prepared as reported earlier [8, 9]. The commercial sample of PABA is recrystallized from water and its standard solution (~0.01 M) was prepared in water. For two ointments of PABA available in the local market, namely Paraminol and Melanocyl, the

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active substance was extracted by dispersing known amounts (~0.3 g) in water (75 ml). These were filtered quantitatively and the filtrate and washings were made up to definite volumes (250 ml) with water. Amaranth (0.1%) and starch (0.2%) indicator solutions were prepared in water [13].

*Procedures*

(i) *Direct potentiometric method.* A measured volume (5–15 ml) of PABA solution was diluted to 50 ml with 10% (v/v) aqueous acetic acid and titrated with standard NBSA. Near the equivalence point, the addition of NBSA was restricted to 0.1 ml and the solution was stirred for 30 s before taking the steady potential in each time. The titration was continued until there was no significant change in potential on further addition of oxidant.

(ii) *Direct visual method.* To a measured volume (5–15 ml) of PABA solution, two drops of amaranth indicator were added and the solution was diluted to 100 ml with 50% (v/v) aqueous acetic acid. The solution was titrated with standard NBSA solution until the discharge of the red colour of the solution. A blank titration was carried out in each time and no blank correction was found to be necessary.

From the titre values the weight of PABA in the drug solution was calculated using the equation,

$$\text{weight of PABA} = \frac{M \times V \times N}{n} \text{ mg},$$

where $M$ is the molecular weight of PABA, $V$ is the volume of NBSA of strength $N$, and $n$ is the number of equivalents of NBSA consumed per mole of PABA (4 in the present case).

(iii) *Excess-back method.* To a measured volume (20 ml) of NBP or NBSA, an aliquot (5–15 ml) of PABA solution was added in an iodine flask. The flask was stoppered well and kept for 30 min in the case of NBP, and for 15 min in the case of NBSA. Then 10 ml of 10% potassium iodide solution was added and the liberated iodine was titrated with standard sodium thiosulphate solution using starch indicator. A blank titration was also carried out in each case. From the titre values the weight of PABA in the drug was calculated using the equation,

$$\text{weight of PABA} = \frac{M(V_2 - V_1) \times N}{n} \text{ mg},$$

where $M$ is the molecular weight of PABA, $V_2$ the volume of sodium thiosulphate for the blank, $V_1$ the volume of sodium thiosulphate for the sample, $N$ the normality of sodium thiosulphate, and $n$ is the number of equivalents of NBP or NBSA consumed per mole of PABA.

## Results and Discussion

The results of the titrations are presented in Tables 1 and 2. In these reactions PABA is either tribrominated (by excess-back titrations with both NBP and NBSA) or

**Table 1**
Excess-back titrations of PABA and its ointments using NBP and NBSA

| Substance | Range studied (mg) | Maker's specification (%) | PABA found* Using NBP Recovery (%) | Using NBP C.V. (%) | Using NBSA Recovery (%) | Using NBSA C.V. (%) | Using brominating mixture Recovery (%) | Using brominating mixture C.V. (%) |
|---|---|---|---|---|---|---|---|---|
| PABA (pure sample) | 8.8–13.2 | — | 99.9 | 1.8 | 99.7 | 0.2 | 98.8 | 1.8 |
| Paraminol | 5.8–16.5 | 10 | 9.9 | 2.0 | 9.9 | 0.7 | 11.2 | 5.2 |
| Melanocyl | 5.8–11.5 | 2 | 2.4 | 4.9 | 2.3 | 0.9 | 2.6 | 7.0 |

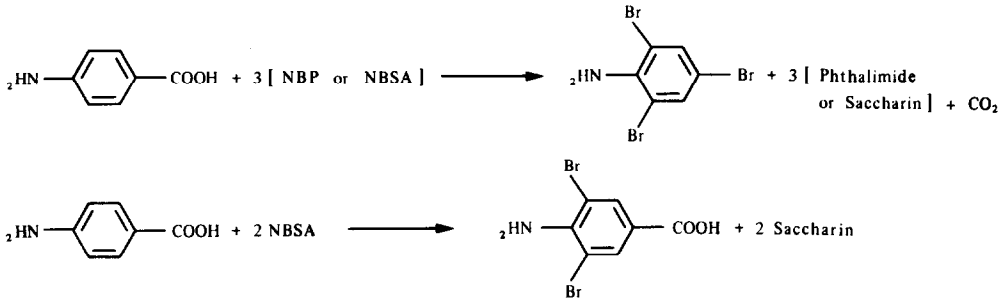
*Average of 10 replicates.

**Table 2**
Direct titrations of PABA and its ointments using NBSA

| Substance | Range studied (mg) | Maker's specification (%) | PABA found* Visual method Recovery (%) | C.V. (%) | Potentiometric method Recovery (%) | C.V. (%) |
|---|---|---|---|---|---|---|
| PABA (pure sample) | 6.8–13.2 | — | 100.1 | 0.3 | 100.1 | 0.3 |
| Paraminol | 5.8–16.5 | 10 | 9.6 | 1.7 | 9.5 | 0.4 |
| Melanocyl | 5.8–16.5 | 2 | 2.4 | 5.3 | 2.4 | 1.3 |

*Average of 10 replicates.

dibrominated (by direct titrations with NBSA). The reactions are quantitative and the equivalent weights ($M/2$) of NBP and NBSA are 113 and 131, respectively. The tribromination is complete in 15 min with NBSA, and in 30 min with NBP, suggesting that the former is a better brominating agent than the latter. During the titrations NBP is reduced to phthalimide and NBSA to saccharin [7, 8]. PABA consumed 6 equivalents of NBP and NBSA in the excess-back method and 4 equivalents of NBSA in the direct titration method as per the equations given below:




*Product analysis*

The products were prepared as per the titration procedures, in large quantities and recrystallized from aqueous alcohol. Percentage of bromine in the reaction product of PABA and the titrant in the excess-back method (**A**) and in the direct method (**B**) was determined by Volhard's method. It was found that **A** contained 72.3% of bromine and **B** contained 54% of bromine confirming the presence of three and two bromine atoms, respectively. The product **A** did not give any effervescence with sodium bicarbonate and the IR spectrum showed no sharp peak at 1600 $cm^{-1}$. This was in accordance with the fact that the —COOH group of PABA was replaced by one bromine atom. The $—NH_2$ group being *ortho–para* directing, the other two bromine atoms were attached to the two *ortho* positions with respect to the $—NH_2$ group. This was actually proved by the fact that the melting point of product **A** (119°C) was found to be identical with the melting point of 2,4,6-tribromoaniline (120°C). Furthermore, the IR spectra of the prepared 2,4,6-tribromoaniline and the reaction product **A** were identical.

The IR spectrum of product **B** showed a sharp peak at 1600 $cm^{-1}$ and the compound gave effervescence with sodium bicarbonate solution, confirming the presence of the —COOH group in the compound. Finally, the melting point of **B** (330°C) was found to be identical with the melting point of 3,5-dibromo-4-aminobenzoic acid [14]. Hence

product **A** was 2,4,6-tribromoaniline, and product **B** was 3,5-dibromo-4-aminobenzoic acid.

In the direct visual titration with NBSA, the end point is clear when amarath indicator is used (red to colourless). In the potentiometric titration with NBSA, the end point is sharp and a potential jump of about 300 mV is obtained at the equivalence point for the addition of 0.1 ml of 0.01 M NBSA. As for the pure sample of PABA, both the direct visual and the potentiometric methods using NBSA are very precise, but for the formulations, the potentiometric method is more precise than the visual method. With regard to the excess-back titrations, the use of NBSA gives a better precision than that of NBP or other reported methods, both on the pure sample of PABA and its formulations.

Drug excipients like starch, magnesium stearate, talcum and lactose do not interfere with the titrations. Methoxalen generally present along with PABA in the pharmaceutical preparations also does not interfere with the titrations.

The present methods are accurate, precise and superior to the existing methods. The official nitrite titration method [2, 3] is tedious, while for all other bromination methods, potassium bromide needs to be added. Bromometric methods using chloramine-T, Bromamine-B etc. [6] are quantitative only in controlled pH conditions. NBP and NBSA titrations can proceed very well without the addition of any bromide ion and there is no need to control the pH. Hence the present methods are simpler and better than the existing methods for the purpose.

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