Determination of Finasteride, Indapamide and Tiemonium methylsulfate using Surface Plasmon Resonance Band of Silver Nanoparticles

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ABSTRACT
A simple and sensitive method was developed for spectrophotometric determination of finasteride, indapamide and tiemonium methylsulfate in their pure form and in their pharmaceutical formulations. It was found that the studied drugs have the ability to reduce silver nitrate to silver nanoparticles (AgNPs) in the presence of sodium citrate as a stabilizing agent. Silver nanoparticles (AgNPs) produce a very intense surface plasmon resonance peak at 423 nm that allows the quantitative determination of the studied drugs. The calibration curves were linear with concentrations range of 0.50–5.00, 0.50-5.00 and 0.30-2.00 µg/mL for finasteride, indapamide and tiemonium methylsulfate, respectively. The proposed method was successfully applied to the determination of the studied drugs in their pharmaceutical formulations. Furthermore, content uniformity testing of the studied pharmaceutical tablets was also conducted.

KEYWORDS: Silver nanoparticles, Finasteride, Indapamide, Tiemonium methylsulfate.

1.0 Introduction
Finasteride is N-(1,1-Dimethylene)-3-oxo-4-aza-5a-androst-1-ene-17b-carboxamide (Table 1).

Several methods have been reported for finasteride determination including spectrophotometry [3-7], HPLC [8-10], HPTLC [11], voltammetry [12] and polarography [13]. Indapamide is 4-Chloro-N-(2RS)-2-methyl-2,3-dihydro-1H-indol-1-yl]-3-sulphamoylbenzamide (Table 1). The drug exerts diuretic actions similar to thiazide diuretics, despite lacking a thiazide moiety in the drug. It is used for treating hypertension and oedema associated with heart failure [1]. Indapamide is an official drug listed in BP [2] and it can also be determined using HPLC. Different techniques were reported for its determination including spectrophotometry [14-18], chromatographic methods [19-21] and voltammetry [22]. Tiemonium methylsulfate is 4-[3-Hydroxy-3-phenyl-3-(2-thie-
Finasteride was obtained from SIGMA pharmaceutical industries, Egypt. Its purity was found to be 99.92% according to the comparison method [6]. Indapamide was obtained from Pharco pharmaceuticals, Alexandria, Egypt. Its purity was found to be 99.95% according to the comparison method [17]. Tiemonium methylsulfate was obtained from Adwia Pharmaceutical Industries Co., Cairo, Egypt. Its purity was found to be 99.9% as reported by the company. Its purity was found to be 100.40% according to the comparison method [23]. Silver nitrate (AgNO₃) was obtained from Morgan Speciality Chemicals Company and its purity was found to be 99.5% as reported (Batch No 572070216). Sodium citrate was obtained from Fischer Chemical (Fischer scientific UK limited, UK) and Sodium hydroxide was obtained from Alpha Chemicals and was for laboratory use. Its purity was found to be 98% as reported by the company.

2.3 Pharmaceutical Preparations

- Prostride® capsules containing 5 mg finasteride per capsule (obtained from Adwia Pharmaceutical Industries Co., Cairo, Egypt) Batch No. 1603221.
- Hypotense® tablets containing 2.5 mg indapamide per tablet (obtained from the Arab Drug Company, Cairo, Egypt) Batch No. 210189.
- Normaten® tablets containing 2.5 mg indapamide and 50 mg captopril per tablet (obtained from Tenth of Ramadan For Pharmaceutical Industries & Diagnostic Agent (rameda), 6th of October city, Egypt) Batch No. 170439.
- Visceralgine® tablets containing 50 mg tiemonium methylsulfate per tablet (obtained from Sedico Pharmaceutical Company, Giza, Egypt) Batch No. 0916299.
- Viscera® ampoules, containing 5 mg tiemonium methylsulfate per 2 mL (Sedico Pharmaceutical Company, Giza, Egypt), Batch No. 1216287/A.

2.4 Standard Solutions

2.4.1 Standard Stock Solution

A standard stock solution containing 1 mg/mL of each drug was prepared separately in ethanol, methanol, and water for finasteride, indapamide and tiemonium methylsulfate, respectively.

2.4.2 Working Standard Solutions

The standard stock solution of each drug was diluted separately, by the same solvent of each drug, to obtain a concentration of 10 µg/mL.
2.5 General Procedures
In a 5 mL volumetric flask appropriate amounts of silver nitrate, sodium citrate, drugs (finasteride, indapamide, tiemoni um methylsulfate), and sodium hydroxide, only for finasteride, were added to make up the volume with distilled water. Each solution was heated in water at a suitable temperature for appropriate times. Absorbance was measured at the suitable wavelength against reagent blank treated similarly (Table 2).

2.6 Assay of Pharmaceutical Preparations Assay
2.6.1 Tablets Assays
2.6.1.1 Assay of Hypotense® and Normaten® Tablets
Ten tablets were weighed and pulverized. Then, the powder accounting for 10 mg of drugs was transferred into a 10 mL volumetric flask. The powder was dissolved using 1 mL of 0.05M HCl and diluted to mark using methanol. Solutions were filtered and neutralized with 1 mL of 0.05 M NaOH and diluted to 10 µg/mL. Aliquots from this solution were used for subsequent experiments.

2.6.1.2 Assay of Visceralgine® tablets
Ten tablets were weighed, pulverized into a fine powder, in a 10 mL volumetric flask specific quantity of powdered tablets equivalent to 10.0 mg pure drugs were dissolved, diluted to mark using methanol and sonicated for 30 minutes. Solutions were filtered and then further diluted to 10 µg/mL. Aliquots from this solution were used for subsequent experiments.

2.6.2 Assay of Prostride® capsules
The contents of ten capsules were emptied in a 10 mL volumetric flask and accurately weighed the amount of finasteride equivalent to 10 mg was dissolved and diluted to the mark using ethanol. The drug solution was filtered and further diluted to 10 µg/mL and aliquots from this solution were used for subsequent experiments.

2.6.3 Assay of Viscera® ampoule
Specific volumes of ampule solutions equivalent to 10.0 mg pure drug were placed in a 100.0 mL volumetric flask, diluted to 100.0 mL with 50% methanol (v/v). The drug solution was then diluted to 10 µg/mL and aliquots from this solution were used for subsequent experiments.

2.7 Procedures for Content Uniformity Testing
Each of the ten tablets of Hypotense®, and capsules of Prostr ider® were weighted accurately. Each tablet or capsule was considered a sample and analyzed as previously mentioned (section 2.6). The content of the drug present in the tablets was calculated as a percent of the label claim for each tablet or capsule, respectively. The percent drug content of the label claim was assessed to see if it complied with the acceptance criteria.

2.7.1 Procedures for application of tiemoni um methyl sulfate into plasma
In a centrifuge tube were 0.5 mL of 20 µg/mL tiemonium methylsulfate mixed with 0.5 mL of plasma using vortexing.

| Parameter                        | Finasteride | Indapamide | Tiemonium methylsulfate |
|----------------------------------|-------------|------------|-------------------------|
| λ max (nm)                       | 422         | 423        | 423                     |
| Concentration of AgNO₃ (M)       | 0.01        | 0.002      | 0.015                   |
| Volume of AgNO₃ (mL)             | 0.40        | 1.00       | 0.30                    |
| Concentration of sodium citrate (w/v %) | 0.2%       | 0.2%       | 1%                      |
| Volume of sodium citrate (mL)   | 0.10        | 0.40       | 0.50                    |
| Concentration of NaOH (M)        | 0.001       | n.a.       | n.a.                    |
| Volume of NaOH (mL)              | 0.10        | n.a.       | n.a.                    |
| Temperature(°C)                  | 95.00       | 85.00      | 100.00                  |
| Time of heating (min)            | 50.00       | 25.00      | 20.00                   |
| n.a. = not applicable.           |             |            |                         |
Thereafter, 4.0 mL of acetonitrile were added to the tube, mixed well for 1 minute and centrifuged for 30 min at 5000 rpm. The supernatant was passed through a cellulose acetate syringe filter. In 5 mL volumetric flask, 0.15 mL of the supernatant was added to different concentrations of pure drug. The procedures were completed as previously mentioned under general procedures (section 2.5).

3.0 Results and Discussion
In recent years, silver nanoparticles have been reported in many applications. They have gained much interest in chemical analysis due to their high extinction coefficient and cost-effectiveness of the analysis. In an alkaline medium; silver nitrate was reduced by the studied drugs into silver nanoparticles which were stabilized by a sodium citrate solution (Figure 1). Silver nanoparticles exhibit a well-known absorption band at 423 nm that has successfully been utilized in the determination of the cited drugs Figure 1.

3.1 Optimization of experimental variables
3.1.1 Effect of silver nitrate
In order to find the optimum concentration of silver nitrate, different concentrations from 0.5 to 30 mM were examined as shown in Figures 2, 3 and Table 2.

3.1.2 Effect of Stabilizer type and concentration
Stabilization of silver nanoparticles is very important to prevent their aggregation. Nanoparticles stabilization is achieved by two mechanisms: electrostatic- and steric stabilization. Electrostatic stabilization is caused by the repulsion between particles, (e.g. sodium citrate) while steric stabilization is achieved by surrounding the metal center by surfactants or polymers (e.g. PVP). In this study polyvinyl pyrrolidone (PVP), sodium citrate, sodium dodecyl sulphate (SDS), cetyl

Figure 1. Absorbance spectra of the silver nanoparticles formed in the presence of: 4 µg/mL finasteride, 1.8 µg/mL indapamide and 1.25 µg/mL tiemonium methylsulfate.

Figure 2. Effect of concentration of silver nitrate solution on the absorbance of silver nanoparticles formed through reaction of sodium citrate and NaOH solution in presence of 4 µg/mL finasteride, 4.5 µg/mL indapamide and 2 µg/mL tiemonium methylsulfate.

Figure 3. Effect of volume of silver nitrate solution on the absorbance of silver nanoparticles formed through reaction of sodium citrate and NaOH solution in presence of 4 µg/mL finasteride, 4.5 µg/mL indapamide and 2 µg/mL tiemonium methylsulfate.
trimethyl ammonium bromide (CTAB) and methyl cellulose were tried as a stabilizing agent. Sodium citrate was selected as the best stabilizer for the prevention of AgNPs agglomeration Figure 4-6 and Table 2.

3.1.3 Effect of NaOH concentration
There was an increase observed in the absorbance by increasing NaOH concentration until a concentration of 0.001 M. Beyond this concentration, addition of NaOH showed decrease in the absorbance, and formation of black precipitates, most likely due to formation of silver oxide. The explanation of this observation can be as follow; the reaction between analyte and silver nitrate results in the formation of protons, as a result, the removal of these protons can enhance the formation of AgNPs (Figures 7, 8 and Table 2).

3.1.4 Effect of temperature and time of heating
It was observed that the reaction rate increased with increasing temperature. Heating the solution in a water bath at 95°, 85° and 100°C for 50, 25 and 20 min was sufficient to produce maximum color intensities for finasteride, indapamide and tiemonium methylsulfate respectively. (Figures 9, 10 and Table 2).

3.1.5 Order of addition
The sequence of the addition of reactants could influence the rate of silver nanoparticles formation. Out of several reagents studies, the most suitable sequence was drug, sodium citrate, silver nitrate then NaOH for finasteride, drug, sodium citrate then silver nitrate for Indapamide while silver nitrate, sodium citrate, drug for tiemonium methylsulfate (Figure 11).

3.2. Method validation
Method validation was performed according to the ICH guidelines [35].

3.2.1 Linearity
The linearity range of the cited drugs was (0.50-5.0 µg/mL), (0.50-5.0 µg/mL) and (0.30-2.0 µg/mL) for finasteride, indapamide and tiemonium methylsulfate respectively. Regression equation parameters were calculated. The small values of intercepts, relative standard deviation, standard
Figure 5. Effect of concentration of sodium citrate solution on the absorbance of silver nanoparticles formed through reaction of silver nitrate and NaOH solution in presence of 4 µg/mL finasteride, 4.5 µg/mL indapamide and 2 µg/mL tiemonium methylsulfate.

Figure 6. Effect of volume of sodium citrate solution on the absorbance of silver nanoparticles formed through reaction of silver nitrate and NaOH solution in presence of 4 µg/mL finasteride, 4.5 µg/mL indapamide and 2 µg/mL tiemonium methylsulfate.

Figure 7. Effect of concentration of NaOH solution on the absorbance of silver nanoparticles formed through reaction of silver nitrate and sodium citrate solution in presence of 4 µg/mL finasteride.

Figure 8. Effect of volume of NaOH solution on the absorbance of silver nanoparticles formed through reaction of silver nitrate and sodium citrate solution in presence of 4 µg/mL finasteride.
error and high value of correlation coefficient indicated good linearity of the method. All these data were listed in Tables 3 and 4.

3.2.2 Sensitivity
The LOD and LOQ were calculated according to the following equation: LOD = 3.3*(σ/s) and LOQ = 10*(σ/s), where, σ = the standard deviation of blank and s = slope of the calibration curve. Their values were listed in Table 3 indicating the sensitivity of the proposed method.

3.2.3 Accuracy and precision
3.2.3.1 Accuracy
To ascertain the accuracy of the proposed method, the obtained results were compared with the reported methods. Statistical comparison of the results was performed using student t-test and F-test at 95% confidence level Table 5. No significant differences were found between the proposed methods and the reported ones.

3.2.3.2 Precision
Precision was determined by analyzing three different concentrations of each drug three successive times in the same day (intra-day). The same concentrations were assayed on three different days (inter-day). The relative standard deviation and percentages relative error (Er%) were calculated using the following equation:

\[ Er\% = \left(\frac{\text{found} - \text{added}}{\text{added}}\right) \times 100\% \]

Good results and acceptable relative standard deviations were obtained (Table 6).

3.2.4 Selectivity
The selectivity of the method was checked by analyzing different mixtures of the cited drugs with some common excipients as lactose, sodium dodecyl sulphate, calcium carbonate, sodium chloride, sucrose, magnesium stearate and talc. Results showed some interferences from the presence of magnesium stearate which could be overcome by extraction with methanol for indapamide and tiemonium methylsulfate or ethanol for finasteride for tablets filtration Table 7.

3.2.5 Robustness and ruggedness
Robustness was examined by evaluating the effect of small variations in the experimental parameters on the analytical performance of the proposed method. The variation of the studied parameters were analyzed according to the following: volume of silver nitrate solution (0.45, 0.40, 0.35 for finasteride, 1.1, 1.0, 0.9 mL for indapamide, 0.35, 0.30, 0.25
Table 4. Determination of Finasteride, Indapamide and Tiemonium methylsulfate through silver nanoparticles formation.

| Drug               | Finasteride | Indapamide | Tiemonium methylsulfate |
|--------------------|-------------|------------|-------------------------|
|                    | Taken µg/mL | Recovery*  | Taken µg/mL | Recovery*  | Taken µg/mL | Recovery*  |
| 0.50               | 99.60       |            | 0.50        | 100.98     | 0.30        | 99.29      |
| 1.00               | 100.10      |            | 1.00        | 100.98     | 0.50        | 98.81      |
| 2.00               | 99.09       |            | 2.00        | 99.89      | 0.60        | 100.20     |
| 2.50               | 101.41      |            | 3.00        | 99.53      | 0.90        | 100.51     |
| 3.00               | 99.60       |            | 3.50        | 99.74      | 1.00        | 100.57     |
| 3.50               | 99.74       |            | 4.00        | 99.48      | 2.00        | 99.83      |
| 5.00               | 100.00      |            | 4.50        | 100.49     |             |            |
|                    | 5.00        |            | 100.22      |            |             |            |
| Mean*±SD           | 99.93±0.727 | 100.16±0.604 | 99.87±0.702 |
| N                  | 7           | 8          | 6           |
| V                  | 0.529       | 0.365      | 0.493       |
| R.S.D.             | 0.728       | 0.603      | 0.703       |
| S.E.               | 0.275       | 0.214      | 0.287       |
| * Mean of three different experiments

Table 5. Statistical analysis of results obtained by the proposed and the comparison methods.

| Drug               | Finasteride | Indapamide | Tiemonium methylsulfate |
|--------------------|-------------|------------|-------------------------|
|                    | Items       | Proposed method | Comparison method [6] | Proposed method | Comparison method [17] | Proposed method | Comparison method [23] |
| Mean±SD            | 99.93±0.727 | 99.92±0.731 | 100.16±0.604 | 99.95±0.652 | 99.87±0.702 | 100.40±0.753 |
| Variance           | 0.529       | 0.535      | 0.365       | 0.426      | 0.493      | 0.567      |
| N                  | 7           | 5          | 8           | 5          | 6          | 6          |
| Student-t-test     | 0.023(2.228)* | -     | 0.591(2.201)* | -     | 1.261(2.228)* | -     |
| F-test             | 1.011(4.53)* | -          | 1.167(4.12)* | -          | 1.150(5.05)* | -          |
| *Theoretical values of t and F at p = 0.05
Table 6. Precision data for the determination of the cited drugs by the proposed method.

| Drugs              | Intra-day | Inter-day |
|--------------------|-----------|-----------|
|                    | Added     | Found±SE  | Recovery% | RSD% | Er% | Found±SE  | Recovery% | RSD% | Er% |
| Finasteride        | 2.00      | 2.000±1.030 | 100.02 | 1.784 | 0.02 | 1.940±1.109 | 97.00 | 1.980 | -3.00 |
|                    | 3.00      | 3.023±1.213 | 100.77 | 2.085 | 0.77 | 3.015±1.245 | 100.49 | 2.145 | 0.49 |
|                    | 5.00      | 4.899±1.236 | 97.99 | 2.185 | -2.01 | 4.866±1.209 | 97.32 | 1.209 | -2.68 |
| Indapamide         | 1.00      | 1.033±1.187 | 100.25 | 2.050 | 0.25 | 1.004±0.829 | 100.43 | 2.182 | 0.43 |
|                    | 3.00      | 2.980±1.271 | 99.35 | 2.216 | -0.65 | 2.990±1.255 | 99.65 | 2.182 | -0.35 |
|                    | 5.00      | 5.047±0.958 | 100.94 | 1.643 | 0.94 | 5.052±1.232 | 101.05 | 2.112 | 0.57 |
| Tiemonium methylsulfate | 0.50       | 0.497±1.104 | 99.35 | 1.924 | -0.65 | 0.500±1.168 | 100.02 | 2.022 | 0.02 |
|                    | 1.00      | 1.006±1.168 | 100.57 | 2.011 | 0.57 | 1.006±1.284 | 100.57 | 2.212 | 0.57 |
|                    | 2.00      | 2.015±1.046 | 100.77 | 1.799 | 0.77 | 2.010±0.892 | 100.50 | 1.537 | 0.50 |

Table 7. Analysis of the cited drugs by the proposed method in presence of some common excipients.

| Tolerance Molar ratio (M:M)* | Recovery %** |
|------------------------------|--------------|
|                              | Finasteride  | Indapamide  | Tiemonium methylsulfate |
| Lactose                      | Sodium dodecylsulfate  | Lactose | Calcium carbonate | Lactose | Sodium chloride | Sucrose |
| 1:1                          | 99.09 | 101.61 | 98.53 | 102.75 | 100.51 | 97.14 | 98.26 |
| 1:10                         | 95.32 | 100.35 | 95.01 | 103.88 | 99.61 | 96.91 | 99.61 |
| 1:50                         | 96.58 | 101.61 | 95.28 | 103.43 | 98.26 | 96.01 | 100.51 |
| 1:100                        | 97.08 | 98.84 | 100.16 | 102.75 | 96.69 | 95.11 | 103.65 |
| Other excipients             | Finasteride  | Indapamide  | Tiemonium methylsulfate |
| Magnesium stearate (40 µg/ml) | 94.06 | 93.11 | 93.76 |
| Talc (40 µg/ml)              | 99.09 | - | 102.75 |

*Drug: excipients; finasteride 2 µg/mL (5.3x10^-4 M), indapamide 2 µg/mL (5.4x10^-4 M) and tiemonium methyl sulfate 0.9 µg/mL (2x10^-4 M); ** Mean of three determinations.

Table 8. Method robustness and ruggedness expressed as (recovery %RSD).

| Drugs               | Taken µg/mL | Volume of silver nitrate solution | Volume of sodium citrate | Volume of NaOH | Inter-instruments (n=2) |
|---------------------|-------------|----------------------------------|--------------------------|---------------|------------------------|
| Robustness Parameters altered | JENWAY6715UV/Vis. | ShimadzuUV1800 PC |
| Finasteride         | 3.50        | 99.26±0.836 | 98.30±1.462 | 101.32±1.636 | 100.46±1.012 |
| Indapamide          | 3.00        | 100.49±1.226 | 98.50±0.943 | - | 98.62±1.297 |
| Tiemonium methylsulfate | 0.90       | 99.01±1.511 | 100.58±1.569 | - | 99.49±1.757 |
### Table 9. Application of the proposed method for determination of the cited drugs in their pharmaceutical formulations.

| Drugs          | Prostride® capsules | Hypotense® tablets | Normaten® tablets |
|----------------|---------------------|--------------------|-------------------|
|                | Taken µg/mL | Added µg/mL | Recovery* % | Taken µg/mL | Added µg/mL | Recovery* % | Taken µg/mL | Added µg/mL | Recovery* % |
| Statistics     |            |            |            |            |            |            |            |            |            |
|                | 1.00       | -          | 100.10     | 1.00       | -          | 98.81      | 1.00       | -          | 96.09      |
|                | 1.25       | 102.21     |             | 2.00       | 98.53      |             | 1.00       | 97.18      |
|                | 1.50       | 103.62     |             | 2.50       | 99.46      |             | 2.50       | 97.50      |
|                | 2.25       | 101.50     |             | 3.00       | 100.25     |             | 3.00       | 97.54      |
|                | 2.75       | 102.25     |             | 3.50       | 99.89      |             | 4.00       | 96.91      |
|                | 3.00       | 103.79     |             | 4.00       | 100.98     |             |             |            |
| Mean S.D.      | 102.67±0.990| 99.82±0.911| 97.28±0.299|
| N              | 5          | 5          | 4          |
| V              | 0.979      | 0.829      | 0.089      |
| S.E            | 0.443      | 0.407      | 0.134      |
| * Mean of three different experiments |

### Table 10. Determination of tiemonium methylsulphate in its pharmaceutical formulations and in plasma sample.

| Visceralgin* tablets | Visceralgin * ampoule | Plasma sample |
|---------------------|-----------------------|---------------|
| Taken µg/mL | Added µg/mL | Recovery* % | Taken µg/mL | Added µg/mL | Recovery* % | Taken µg/mL | Added µg/mL | Recovery* % |
| 0.30     | -          | 102.66     | 0.30       | -          | 99.29      | 0.30       | -          | 97.27      |
| 0.30     | 100.64     |             | 0.40       | 99.75      |             | 0.30       | 97.94      |
| 0.60     | 98.52      |             | 0.50       | 101.23     |             | 0.60       | 96.16      |
| 0.70     | 100.33     |             | 0.70       | 100.91     |             | 0.70       | 95.71      |
| 0.80     | 101.69     |             | 0.90       | 101.85     |             | 0.80       | 96.13      |
| 1.50     | 101.42     |             | 1.30       | 98.14      |             | 1.70       | 97.58      |
| 1.60     | 101.40     |             | 1.40       | 98.86      |             |            |            |
| Mean S.D. | 100.67±1.175| 100.46±1.036| 98.70±0.990|
| N         | 6          | 6          | 5          |
| V         | 1.380      | 1.074      | 0.979      |
| S.E       | 0.480      | 0.423      | 0.404      |
| * Mean of three different experiments |
Table 11. Results of content uniformity testing of finasteride and indapamide tablets using the proposed methods.

| Parameter | Percentage of the label claim |
|-----------|-----------------------------|
| Finasteride | Indapamide |
| 96.13 | 99.21 |
| 97.33 | 102.94 |
| 97.73 | 102.67 |
| 104.00 | 96.19 |
| 102.67 | 95.00 |
| 96.00 | 104.64 |
| 98.80 | 99.68 |
| 101.47 | 103.68 |
| 103.20 | 95.65 |
| 97.87 | 99.56 |

Mean (X) | 99.52 | 99.99 |
S.D. | 3.03 | 3.57 |
% RSD | 3.04 | 3.57 |
% Error | 0.96 | 1.13 |
Acceptance value (AV) | 7.26 | 8.56 |
Max. allowed AV (L1) | 15 | 15 |

Figure 12. Effect of order of addition of silver nitrate, sodium citrate and NaOH solutions to: 4 μg/mL finasteride, 4.5 μg/mL indapamide and 2 μg/mL tiemonium methylsulfate. D=drug, Ag=silver nitrate, SC=sodium citrate.

3.3 Analytical applications

In the assay of Hypotense® and Normaten® tablets, first, we got a low recovery of indapamide but when we used 1.0 mL of 0.05 M HCl in dissolution medium, we got satisfactory results. This can be explained by a paper published by Nishath Fathima et al [36]. They studied mechanisms of drug excipient interaction showing that a physical interaction occurs between primary amine drugs, indapamide, and microcrystalline cellulose, an excipient in its tablet dosage forms. For low dose drugs, it can lead to dissolution failures and this can be remedied by carrying out dissolution using 0.05 M HCl). The proposed method was applied to determine the studied drugs in their pharmaceutical dosage forms with satisfactory results obtained. Also spiking of tiemonium methyl sulphate into plasma and good extraction from it proved the suitability of the proposed method Figure 12, Table 9-10.

3.4 Content Uniformity Test
Due to the sensitivity of the proposed method, the method is ideally suited for content uniformity testing. The steps of the test were adopted according to the USP [37] procedure. The acceptance value (AV) was calculated and it was found to be smaller than the maximum allowed acceptance value (L1). The results demonstrated drug uniformity for finasteride and indapamide as shown in Table 11.

4.0 Conclusion
Application of silver nanoparticles as a chromogenic agent has been demonstrated in this work for optical determination of finasteride, indapamide and tiemonium methylsulfate. The proposed method was found to be simple, sensitive and easily applicable to the analysis of the cited drugs in their pharmaceutical dosage forms with good accuracy and precision. The method is based on the reduction of $\text{AgNO}_3$ by the cited drugs.

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