Spectrophotometric determination of buspirone HCl and doxazosin mesylate using citrate-capped silver nanoparticles

Magda Mohamed Ayad,
Hisham Ezzat Abdellatef,
Mervat Mohamed Hosny
and Naglaa Abdel-Sattar Kabil*

Faculty of Pharmacy,
Analytical Chemistry Department,
Zagazig University,
Zagazig, 44519, Egypt
Email: mermaka89@yahoo.com
Email: ezzat_hisham@yahoo.com
Email: hmervat20@yahoo.com
Email: nagla_kabil@yahoo.com
*Corresponding author

Abstract: A simple and rapid spectrophotometric method was developed for determination of buspirone HCl and doxazosin mesylate in bulk and pharmaceutical formulations. In this paper silver nanoparticles (Ag-NPs) were prepared chemically using sodium citrate as reducing and stabilising agent. Silver nanoparticles showed an absorption band at 420 nm. Aggregation of citrate stabilised silver nanoparticles (Ag NPs) were used for quantitative determination of the studied drugs with formation of a new red shifted band at 545, 690 nm for buspirone HCl and doxazosin mesylate respectively. Different experimental factors were optimised and the calibration curves were linear with concentrations of (0.10-0.60 μg/mL), (5.0-14.0 μg/mL) for buspirone HCl and doxazosin mesylate respectively. Validation of the analytical performance of the method was carefully investigated, and the results were satisfactory.

Keywords: silver nanoparticles; buspirone HCl; doxazosin mesylate; spectrophotometric; determination; aggregation; pharmaceutical formulations.

Reference to this paper should be made as follows: Ayad, M.M., Abdellatef, H.E., Hosny, M.M. and Kabil, N.A-S. (2021) 'Spectrophotometric determination of buspirone HCl and doxazosin mesylate using citrate-capped silver nanoparticles', *Int. J. Nanomanufacturing*, Vol. 17, No. 1, pp.13–25.

Biographical notes: Magda Mohamed Ayad is Professor of Analytical Chemistry Department, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt.

Hisham Ezzat Abdellatef is Professor of Analytical Chemistry Department, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt.

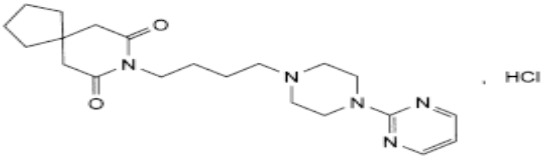
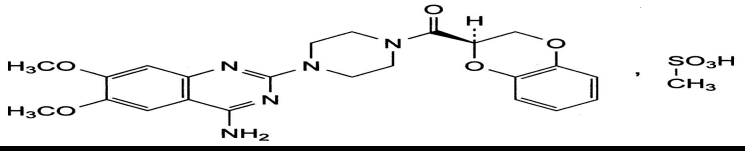
Mervat Mohamed Hosny is Professor of Analytical Chemistry Department, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt.

Naglaa Abdel-Sattar Kabil is an Assistant Lecturer of Analytical Chemistry Department, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt.

1 Introduction

Buspirone HCl is 8-[4-[4-(Pyrimidin-2-yl) piperazin-1-yl] butyl]-8-azaspiro [4.5] decane-7, 9-dione hydrochloride (Table 1). It is an anxiolytic agent from the azapirone class of compounds (Sweetman, 2009). Buspirone hydrochloride is official and can be determined by non-aqueous titration with perchloric acid and the end-point determined potentiometricaly (Gaur et al., 2013) and by HPLC method for its assay (Rockville, 2007). Various analytical methods have been applied for its determination in raw material, pharmaceuticals and biological fluids. These methods include chromatography (Kim et al., 2016), spectroflourimetry (Jose et al., 2012), and spectrophotometry (Youssef et al., 2006; Zayed and El-Habeeb, 2009; Kurien et al., 2012a).

Table 1 Chemical structure of the studied drugs

Buspirone HCl	
Doxazosin mesylate	

Doxazosin mesylate is 1-(4-Amino-6, 7-dimethoxyquinazolin-2-yl)-4-[(2RS)-2, 3-dihydro- 1, 4 -benzodioxin-2-ylcarbonyl] piperazine methanesulphonate (Table 1). It is used in the management of hypertension, and in benign prostatic hyperplasia to relieve symptoms of urinary obstruction (Sweetman, 2009). Doxazosin is official and can be determined by liquid chromatographic method (Gaur et al., 2013). Different methods were reported for its determination including spectrophotometry (Bebawy et al., 2002; Hashmi et al., 2007; Aydodmup and Barla, 2009), liquid chromatography (Kim et al., 2006; Rao et al., 2007; Erceg et al., 2010) and voltametric method (Altiokka, 2001; Arranz et al., 1997).

In the present work a new colorimetric method was performed for determination of buspirone HCl and doxazosin mesylate in bulk and pharmaceutical formulations. This colorimetric method was convenient for determination of both drugs. AgNPs have a characteristic surface plasmon resonance (SPR) peak appears at 420 nm which could be shifted to higher wavelength upon the interaction with the analyte accompanied by a

change in the colour of the colloidal solution. Citrate-capped AgNPs with negatively charged surface can be symmetrically dispersed in water by the electrostatic repulse interaction of each particle. However, the presence of positively charged molecules would induce the aggregation of AgNPs, causing the colour change of AgNPs suspension from yellow to pink, and then to blue depending on the aggregation degree of AgNPs.

2 Materials and methods

2.1 Instrumentation

A single cell holder JENWAY 6715 UV/Visible spectrophotometer equipped with 10 mm matched quartz cells was employed for all absorbance measurements

2.2 Materials and reagents

All solvents and reagents used were of the highest purity.

- Buspiron HCl (obtained from Sigma pharmaceuticals, Kwesna, Egypt). Its purity was found to be 99.9% as reported from company and 100.20% according to the comparison method.
- Doxazosin mesylate (obtained from EIPICO, Egypt). Its purity was found to be 99.9% as reported from company and 100.40 % according to the comparison method.
- Silver nitrate (obtained from Morgan Specialty Chemicals Company). Its purity was found to be 99.5% as reported from company, Batch No 572070216
- Sodium citrate (obtained from Fischer chemical, Fischer scientific UK limited, UK)
- Water (obtained from Fisher chemical® laboratory reagent grade).

2.3 Pharmaceutical preparations

Buspar® tablets (SmithKline Beecham an affiliated co. to GlaxoSmithKline) batch number 109736, labelled to contain 10 mg Buspirone HCl per tablet.

Cardura ® tablets (Pfizer Egypt S.A.E. Cairo A.R.E. under authority of Pfizer INC., USA) batch number 5202, labelled to contain 4 mg doxazosin mesylate per tablet.

2.4 Standard solutions

Stock standard solutions of 100.0 μg/mL of the cited drugs were prepared by dissolving 10.0 mg of pure drugs in 100.0 mL volumetric flask with distilled water for buspirone HCl, while 100.0 μg/mL doxazosin mesylate was prepared by dissolving 10.0 mg of the pure drug in least amount of methanol then complete to 100.0 mL with distilled water. The stock solution was diluted with distilled water to obtain working standard solutions having the required drug concentrations (0.10–14.0 μg/mL).

2.5 General procedure

2.5.1 Synthesis of silver nanoparticles

Citrate stabilised silver nanoparticles were prepared by reduction of silver salt by 1.0% sodium citrate in which 50.0 mL solution containing 1.0 mM of $AgNO_3$ was prepared and heated. At the boiling point, 5.0 mL of sodium citrate was added to this solution with vigorous stirring and the mixture was further heated for an additional 10 min during which the colour changed to light yellow, indicating the formation of AgNPs. The solution was allowed to cool to room temperature and stored at 4 °C for further use (Sandeep et al., 2017).

2.5.2 Procedures for determination of buspirone HCl and doxazosin mesylate

An appropriate volume of the working drug solution which gave a final concentration of 0.10–14.0 µg/mL of the studied drugs was transferred to 5.0 mL calibrated volumetric flask. Appropriate volumes of Ag NPs solution were added. The solution was mixed thoroughly and allowed to stand for 5 min. Absorbances were measured at suitable λ_{max} against reagent blank treated similarly (Table 2).

Table 2 Analytical parameters for determination of buspirone HCl and doxazosin mesylate using silver nanoparticles

Parameter	*Buspirone HCl*	*Doxazosin mesylate*
λ_{max}(nm)	545	690
Volume of silver nanoparticle	2	1.5
Time(min)	5	5
Temperature	25	25

2.5.3 Assay of pharmaceutical preparations

Ten tablets were accurately weighed and pulverised into fine powder. In 100.0 mL volumetric flask, specific quantity of powdered drugs equivalent to 10.0 mg pure drug were dissolved and diluted to the mark with methanol for doxazosin mesylate and distilled water for buspirone HCl. Solutions were filtered then further dilutions of the filtrate were made to obtain sample solutions in the required final concentrations of 0.10–14.0 µg/mL). Procedures were completed as in general procedures.

3 Results and discussion

Nanoparticles had optical properties that were sensitive to size, shape, concentration, agglomeration state, and refractive index near the nanoparticle surface, which made spectroscopy a valuable tool for identifying, characterising, and studying different materials. Silver nanoparticles (Ag NPs) were another widely studied nanomaterial which gained much interest due to their simplicity, rapidity and they did not need the use of complicated apparatus. Silver nanoparticles were colloidal solutions of yellow colour with absorption band at 420 nm. This yellow solution was synthesised by chemical

reduction using sodium citrate as reducing and stabilising agent. Upon addition of the studied drugs a red-shift in absorption maximum appeared due to aggregation of silver nanoparticles (Figure 1). In the present paper silver nanoparticles were successfully used for determination of buspirone HCl and doxazosin mesylate.

3.1 Characterisation of silver nanoparticles

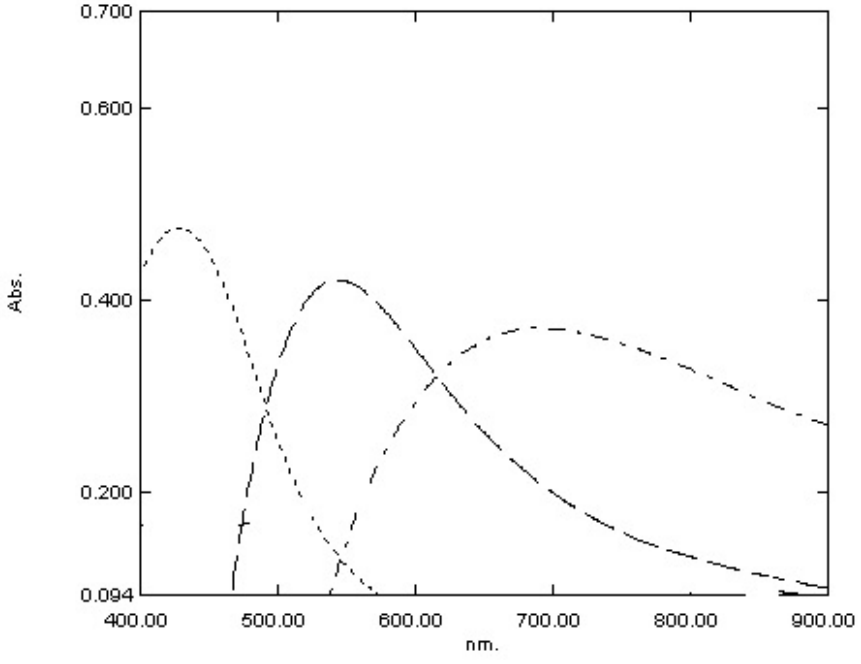
3.1.1 Synthesis of silver nanoparticles

Silver nanoparticles were synthesised by chemical reduction using sodium citrate according to this equation (Piñero et al., 2017):

$$4Ag^{+} + Na_3C_6H_5O_7 \rightarrow 4Ag^{\circ} + C_6H_5O_7H_3 + 3Na^{+} + H^{+} + O_2$$

During the synthesis of the AgNPs by conventional heating it was observed that after addition of citrate, the colour of solution changed from colourless to yellow indicating the formation of colloidal silver. The optimal reaction time was fixed at 6 min; when the time exceed the optimal, the reaction mixture change to greenish grey (Chien et al., 2010).

Figure 1 Absorbance spectra of the reaction between Ag NPs and 0.60µg/mL buspirone HCl (----), 11.0 µg/mL doxazosin mesylate (—·—·) and blank (…..)



3.2 Colorimetric determination of the cited drugs using silver nanoparticles

3.2.1 Optimisation of the reaction conditions

To optimise the sensitivity and selectivity of the method, several factors were studied.

3.2.1.1 Effect of pH

Solutions were tested over the pH range of 2.0–10.0 using different pHs buffer media (acetate buffer, phosphate buffer, chloride buffer and borate buffer. When the pH of the solution was lower than 5.0, silver nanoparticles will aggregate rapidly due to the neutralisation of NPs surface charges. Above pH 6, a slight decrease in the absorbance of the reaction was occurred while the highest absorbance was observed without addition of buffer (Figure 2).

Figure 2 Effect of pH on aggregation rate in the presence of 0.60 µg/mL buspirone HCl and 11.0 µg/mL doxazosin mesylate

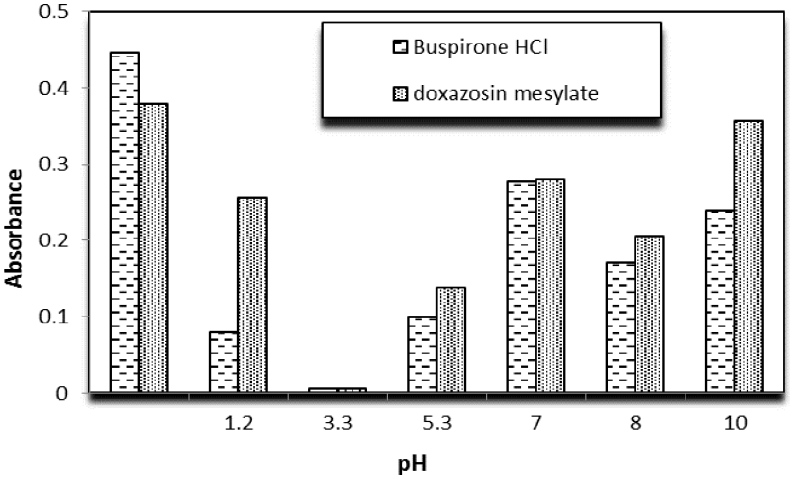
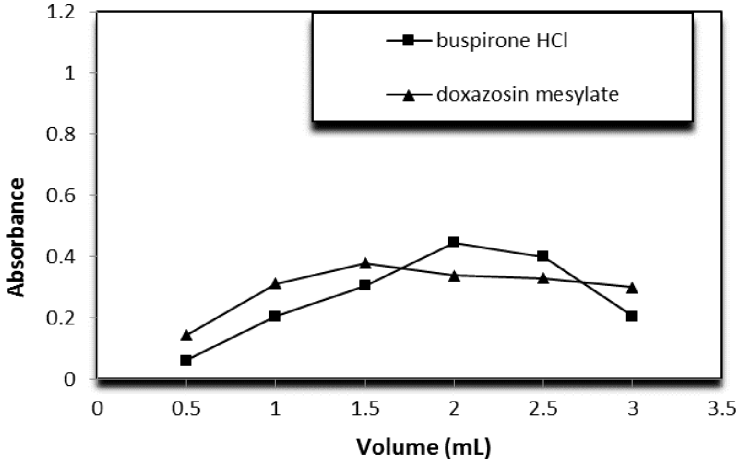


Figure 3 Effect of volume of silver nanoparticles on aggregation rate in the presence of 0.60 µg/mL buspirone HCl and 11.0 µg/mL doxazosin mesylate



3.2.1.2 Effect of volume of silver nanoparticles solution

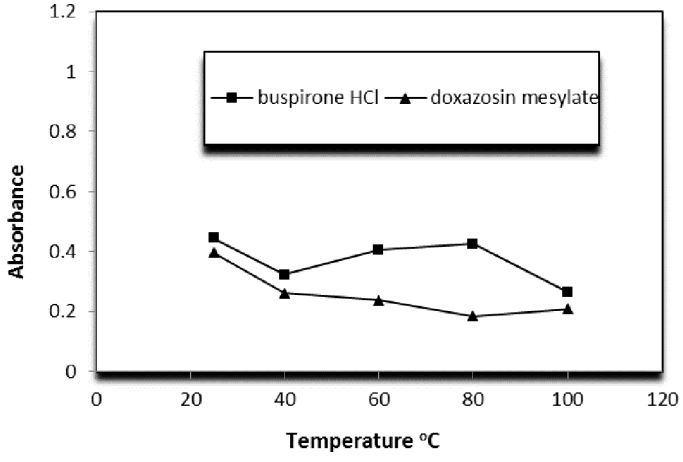
The general analytical procedure was carried out using different volumes of AgNPs solutions. The rate of aggregation increases till 2.0 mL for buspirone HCl and 1.50 mL

for doxazosin mesylate as shown in Figure 3. The absorbance was gradually decreased by increasing the volume of the reagent than this value. This may be attributed to competition of the cited drugs on the binding sites, which results in decreasing the intensity.

3.2.1.3 Effect of temperature

Change in temperature from 25°C to 100°C was studied. A reduction in the absorbance was observed when the reaction was performed at higher temperature hence this reaction was run at room temperature (25°C) (Figure 4).

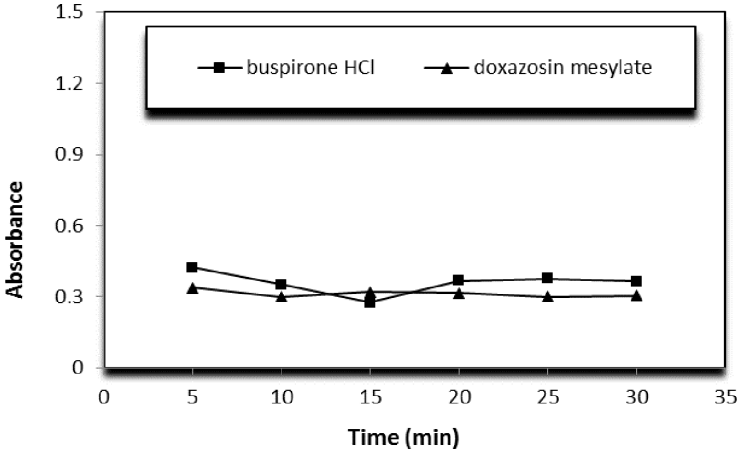
Figure 4 Effect of temperature on aggregation rate in the presence of 0.60 µg/mL buspirone HCl and 11.0 µg/mL doxazosin mesylate



3.2.1.4 Effect of time

Maximum colour intensity was attained at 5 min for the studied drugs (Figure 5).

Figure 5 Effect of time on aggregation rate in the presence of 0.60 µg/mL buspirone HCl and 11.0 µg/mL doxazosin mesylate



3.3 Method validation

3.3.1 Linearity

Under the optimum experimental conditions, standard calibration curves for Ag-NPs aggregation were constructed by plotting absorbances against concentrations. A linear correlation was found. The ranges of concentration, linear regression equations and correlation coefficients for each drug were calculated indicating good linearity over the working concentration range (Tables 3 and 4).

Table 3 Spectral data for determination of cited drugs using silver nanoparticles

Parameter	*Buspirone HCl*	*Doxazosin mesylate*
Linearity range (µg/ml)	0.10–0.60	5.0–14.0
Limit of detection LOD (µg/mL)	0.028	1.43
Limit of quantification LOQ (µg/mL)	0.092	4.75
Regression equation*:		
Slope (b)	0.6849	0.0421
Intercept (a)	0.0338	–0.1098
Correlation coefficient (r)	0.9999	0.9995

*A = a + bc.

Table 4 Assay results for determination of the cited drugs in pure form with silver nanoparticles

	Buspirone HCl		*Doxazosin mesylate*	
	Taken µg/mL	*Recovery* %*	*Taken µg/mL*	*Recovery* %*
	0.10	99.58	5.0	99.67
	0.20	99.43	7.0	99.02
	0.30	100.36	9.0	100.24
	0.40	100.82	10.0	99.95
	0.50	99.34	11.0	101.45
	0.60	100.06	14.0	99.22
Mean ± S.D	99.93 ± 0.584		99.92 ± 0.872	
N	6		6	
V	0.341		0.761	
RSD	0.584		0.873	
SE	0.238		0.356	

*Mean of three different experiments.

3.3.2 Sensitivity

The LOD and LOQ were evaluated using the following equations according to ICH guidelines:

$$LOD = 3.3\frac{\sigma}{s} \qquad LOD = 10\frac{\sigma}{s}$$

where σ = the standard deviation of replicate blank responses (under the same conditions as for sample analysis) and S = the slope of the calibration curve. LODs and LOQs were calculated and listed (Table 3).

3.3.3 Accuracy and precision

3.3.3.1 Accuracy

The accuracy of the proposed method was ascertained by determining pure samples of the cited drugs with reported methods. Statistical analysis of the results obtained by the proposed and comparison methods for the studied drugs showed that no significant differences found between the proposed method and comparison methods. Statistical comparison of the results was performed using Student's t-test and variance ratio F-test at 95% confidence level (Table 5).

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

Drug items	*Buspiron HCl*		*Doxazosin mesylate*	
	Proposed method	*Comparison method*	*Proposed method*	*Comparison method*
Mean ± SD	99.93± 0.584	100.20±0.70	99.92±0.872	100.40±0.753
Variance	0.341	0.49	0.761	0.567
N	6	5	6	6
Student-t-test	0.686(2.282)*	–	1.020(2.228)*	–
F-test	1.437(5.19)*	–	1.342(5.05)*	–

*The corresponding theoretical values for t and F tests at $p = 0.05$.

3.3.3.2 Precision

3.3.3.2.1 Intra-day precision (repeatability)

Intra-day precision was studied by analysis of three different concentrations of pure drugs in triplicate on the same day. The values of relative standard deviation of the suggested method were calculated (Table 6).

3.3.3.2.2 Inter-day precision (intermediate)

The experiment was repeated with the same concentrations on three consecutive days to determine the intermediate precision. The relative standard deviations (RSD %) was calculated at 95% confidence levels. Results of Tables 5 and 6 indicating the validity, applicability of the proposed method and the reproducibility of the results.

Table 6 Precision data for the determination of the cited drugs by the proposed method.

Drug	Added (μg/mL)	Intra-day			Inter-day		
		found ± SE (μg/mL)	Recovery %	RSD%	found ± SE (μg/mL)	Recovery %	RSD%
Buspiron	0.20	0.196±0.843	97.97	1.490	0.200±1.115	100.16	1.928
HCl	0.30	0.299±0.429	99.71	0.746	0.301±1.225	100.36	2.114
	0.50	0.505±0.592	101.00	1.015	0.493±1.196	98.56	2.102
Doxazosin	5.00	5.110±0.963	102.20	1.632	5.047±0.838	100.93	1.438
mesylate	10.00	10.027±0.934	100.27	1.612	10.027±0.934	100.27	1.612
	14.00	13.661±1.334	97.58	2.367	13.724±0.706	98.03	1.248

3.3.4 Selectivity

The effect of commonly utilised excipients was studied. Under the experimental condition employed, to known concentration of the studied drugs, the common excipients lactose, sodium dodecyl sulphate, starch and magnesium stearate were added and analysed. Results showed no interferences from the presence of these excipients (Table 7).

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

Tolerance molar ratio (M:M)	Recovery %**		
	Buspirone HCl	Doxazosin mesylate	
	Lactose	Lactose	Sodium dodecylsulphate
1:1	99.63	100.67	100.67
1:10	98.47	99.95	99.71
1:50	97.88	96.15	97.34
1:100	97.59	95.68	94.73
Other excipients	Buspirone HCl	Doxazosin mesylate	
Magnesium stearate(40μg/mL)	95.25	95.44	
Starch(40μg/mL)	95.55	96.15	

**Mean of three determinations.

3.3.5 Robustness and ruggedness

3.3.5.1 Robustness

Robustness was examined by evaluating the influence of small variations in the experimental parameters on the analytical performance of the proposed method. The studied parameters were silver nitrate and buffer volumes. The effects of the changes were studied on the absorbance by calculating (recovery±%RSD) and these changes had negligible influence on results which provided an indication for the reliability of the proposed method (Table 8).

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

Variation \ *Drugs*	*Buspirone HCl (0.60µg/mL)*			*Doxazosin mesylate (10.0 µg/mL)*		
Volume of silver solution(mL)	1.80	2.0	2.2	1.4	1.5	1.6
Recovery (%)	99.58	100.06	102.74	99.48	99.95	102.09
Mean recovery % ±RSD	100.47 ± 1.145			100.51 ± 1.385		
Ruggedness						
Instruments	*JENWAY6715UV/Vis.*			*-ShimadzuUV1800 PC*		
Statistics \ *Drugs*	*Buspirone HCl (0.60µg/mL)*	*Doxazosin mesylate (10.0µg/mL)*		*Buspirone HCl (0.60µg/mL)*	*Doxazosin mesylate (10.0µg/mL)*	
Recovery (%)	100.06	99.95		101.28	101.14	
Mean recovery %± RSD	100.67± 0.855			100.55 ± 0.835		

Table 9 Application of the proposed method for determination of the cited drugs in their pharmaceutical formulations

Drug	*Buspiron HCl*			*Doxazosin mesylate*		
Statistic	*Taken µg/ml*	*Added µg/ml*	*Recovery* %*	*Taken µg/ml*	*Added µg/ml*	*Recovery* %*
	0.10		96.66	5.0		99.67
		0.10	99.58		5.0	99.67
		0.20	99.43		6.0	100.08
		0.30	100.36		7.0	101.73
		0.40	100.82		8.0	100.89
					9.0	101.56
Mean ± S.D.	100.05 ± 0.656			100.79 ± 0.901		
N	4			5		
V	0.430			0.812		
S.E	0.328			0.403		

*Mean of three different experiments

3.3.5.2 Ruggedness

It was tested by applying the proposed method to the assay of the investigated drugs using the same procedures but using two different instruments. The obtained results were found to be reproducible as shown in Table 8.

3.3.6 Analytical applications

The proposed method was successfully applied to the assay of the studied drugs in their pharmaceutical formulations without interference from common excipients. The validity of the developed method was tested by application of the standard addition technique in which the cited drugs were added to the analysed pharmaceutical dosage forms.

The recovery study showed that the proposed method was accurate and reproducible for both drugs (Table 9).

4 Conclusion

A simple, inexpensive, selective and sensitive colorimetric assay for the determination of buspirone HCl and doxazosin mesylate in bulk and pharmaceutical formulations was developed. This assay was based on aggregation of stabilised silver nanoparticles resulting in red shifted band that used for quantitative determination of the cited drugs. Statistical analysis of the results has been carried out revealing high accuracy and good precision.

References

Altiokka, G. (2001) 'Voltammetric determination of doxazosin in tablets using rotating platinum electrode', *Journal of Pharmaceutical and Biomedical Analysis*, Vol. 25, Nos. 3–4, pp.387–391.

Arranz, A., Fernandez-de-Betono, S., Moreda, J.M., Cid, A. and Arranz, J.F. (1997) 'Cathodic stripping voltammetric determination of doxazosin in urine and pharmaceutical tablets using carbon paste electrodes', *Analyst*, Vol. 122, No. 8, pp.849–854.

Aydodmup, Z. and Barla, A. (2009) 'Spectrophotometric determination of doxazosin mesylate in tablets by ion-pair and charge-transfer complexation reactions', *Journal of AOAC International*, Vol. 92, No. 1, pp.131–137.

Bebawy, L.I., Moustafa, A.A. and Abo-Talib, N.F. (2002) 'Stability-indicating methods for the determination of doxazosin mezylate and celecoxib', *Journal of Pharmaceutical and Biomedical Analysis*, Vol. 27, No. 5, pp.779–793.

Chien, W., Marta, L., Adriana, M. and Liliana, F. (2010) 'Silver Nanoparticles as Optical Sensors', in Perez, D.P. (Ed.): *Silver Nanoparticles*, ISBN: 978-953-307-028-5, InTech, Available from: http://www.intechopen.com/books/silver-nanoparticles/silver-nanoparticles-as-optical-sensors

Erceg, M., Cindric, M., Frketic, L.P., Vertzoni, M., Cetina-Cizmek, B. and Reppas, C. (2010) 'A LC–MS–MS method for determination of low doxazosin concentrations in plasma after oral administration to dogs', *Journal of Chromatographic Science*, Vol. 48, No. 2, pp.114–119.

Gaur, R., Azizi, M., Gan, J., Hansal, P., Harper, K., Mannan, R., Panchal, A., Patel, K., Patel, M., Patel, N., Rana, J. and Rogowska, A. (2013) *British Pharmacopoeia, Volumes II and III*, Her Majesty's Stationery Office, London, UK.

Hashmi, S.S., Channabasavaraj, K.P., Manohara, Y.N., Reddy, Y.R. and Bharatheesha, B.M. (2007) 'Extractive spectrophotometric determination of doxazosin mesylate', *International Journal of Chemical Sciences*, Vol. 5, No. 5, pp.2285–2290.

Jose, K., Thomas, K., Helen, W. and Bijumol, C. (2012) 'Hygeia', *Journal for Drugs and Medicines*, Vol. 4, No. 1, pp.6–14.

Kim, K.T., Lee, J.Y., Park, J.H., Kim, M.H., Kim, J.S., Shin, H.J., Kang, N., Cho, H.J., Yoon, I.S. and Kim, D.D. (2016) 'Development of HPLC method for the determination of buspirone in rat plasma using fluorescence detection and its application to a pharmacokinetic study', *Chemical and Pharmaceutical Bulletin*, Vol. 64, No., pp.1582–1588.

Kim, Y.J., Lee, Y., Kang, M.J., Huh, J.S., Yoon, M., Lee, J. and Choi, Y.W. (2006) 'High-performance liquid chromatographic determination of doxazosin in human plasma for bioequivalance study of controlled release doxazosin tablets', *Biomedical Chromatography*, Vol. 20, No. 11, pp.1172–1177.

Kurien, J., Kurian, T. and Mathew, A. (2012a) 'Simple spectrophotometric determination of buspirone hydrochloride in bulk drug and pharmaceutical dosage forms', *Science and Societ*y, Vol. 10, No. 2, p.147.

Piñero, S., Camero, S. and Blanco, S. (2017) 'Silver nanoparticles: influence of the temperature synthesis on the particles morphology', *Journal of Physics: Conf. Series* 786 012020.

Rao, R.N., Nagaraju, D., Das, A.K. and Jena, N. (2007) 'Separation, characterization, and quantitation of process-related substances of the anti-hypertensive drug doxazosin mesylate by reversed-phase LC with PDA and ESI-MS as detectors', *Journal of Chromatographic Science*, Vol. 45, No. 2, pp.63–69.

Rockville, M.D. (2007) *United States Pharmacopoeia*, XXIV, United States Pharmacopoeia Convention, Washington DC.

Sandeep, K.V., Kuleshwar, P., Kumudini, C., Jyoti, K., Rekha, N., Kallol, K.G. and Manmohan, L.S. (2017) 'Surface plasmon resonance based spectrophotometric determination of medicinally important thiol compounds using unmodified silver nanoparticles', *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Vol. 179, pp.155–162.

Sweetman, S.C. (2009) *Martindale, The Complete Drug Reference*, 36th ed., London (Chicago).

Youssef, R.M., Khamis, E.F., Gazy, A.A., Mahgoub, H. and El-Sayed, M. (2006) 'Assay of buspirone hydrochloride in tablets using kinetic spectrophotometry', *Electrophoresis*, Vol. 11, p.12.

Zayed, M. and El-Habeeb, A.A. (2009) 'Spectroscopic study of the reaction mechanism of buspirone interaction with iodine and tetracyanoethylene reagents and its applications', *Drug Test and Analysis*, Vol. 1, No. 6, pp.267–274.