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O. ZENITA DEVI
K. BASAVAIAH
K.B. VINAY

Department of Chemistry, University of Mysore, Manasagangotri, Mysore, India

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UTILIZATION OF BROMINATION REACTION FOR THE SPECTROPHOTOMETRIC ASSAY OF DOMPERIDONE IN PHARMACEUTICALS

Three simple and sensitive spectrophotometric methods are described for the determination of domperidone (DOM) in bulk drug and in dosage forms using bromate-bromide mixture as brominating agent in acid medium and three dyes, meta-cresol purple (MCP), amaranth (AMR) and erioglaucine (EGC). The methods involve the addition of a known excess of bromate-bromide mixture to an acidified solution of DOM followed by the determination of the residual bromine by reacting with a fixed amount of either MCP dye and measuring the absorbance at 530 nm (method A) or AMR dye and measuring the absorbance at 520 nm (method B) or EGC dye and measuring the absorbance at 630 nm (method C). Beer's law is obeyed over the concentration ranges, 0.63-10.0, 0.25-4.0 and 0.13-2.0 μg mL^{-1} for method A, B and C, respectively. The apparent molar absorptivities are calculated to be 3.751×10^4, 6.604×10^4 and 1.987×10^5 L mol^{-1}cm^{-1} for method A, B and C, respectively, and the corresponding sandell sensitivity values are 0.011, 0.006 and 0.002 μg cm^{-2}. The limit of detection and the limit of quantification are also reported for all the three methods. No interference was observed from common additives found in pharmaceutical preparations. Statistical comparisons of the results with those of the reference method showed excellent agreement, and indicated no significant difference in accuracy and precision. The accuracy and reliability of the methods were further ascertained by performing recovery tests via standard-addition technique.

Key words: domperidon; assay; spectrophotometry; bromate-bromide; dyes; tablets.

Domperidone (DOM), 5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazole-1-yl)propyl]piperidin-4-yl]-1, 3-dihydro-2H-benzimidazol-2-one (Figure 1), is used as an anti-emetic and to suppress nausea and vomiting. DOM is indicated for treating symptoms associated with upper gastrointestinal motility disorders caused by chronic and sub-acute gastritis. It is a gastrointestinal emptying (delayed) adjuvant, a peristaltic stimulant and exhibits antiemetic properties. It can be used in patients with Parkinson's disease [1] and is also found to be effective in the treatment of gastroparesis [2]. It is official in BP [3] which recommends non-aqueous titration with perchloric acid as titrant and naphtholbenzein as indicator.

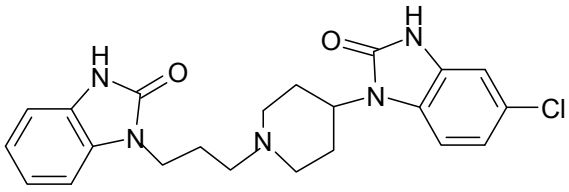

Figure 1. Structure of domperidone.

Several methods have been reported for the determination of domperidone in pharmaceuticals, including differential pulse voltammetry [4], anodic difference pulse voltammetry [5], potentiometry [6], planar chromatography [7], high-performance liquid chromatography [8-19] and high-performance thin-layer chromatography [20-25]. Many of these techniques are deficient in simplicity, cost-effectiveness and easy accessibility.

Spectrophotometry is characterized by its speed and simplicity, accuracy and inexpensive instrument needed, and hence it is an important alternative to other analytical techniques with clear advantages in

Correspondening author: K. Basavaiah, Department of Chemistry, University of Mysore, Manasagangotri, Mysore-570006, India.
E-mail: basavaiahk@yahoo.co.in
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terms of cost of analysis. Rajendraprasad *et al*. [26] have described a UV-spectrophotometric method (λ_{max} = = 284 nm) for DOM in pharmaceuticals. There is only one report on the visible spectrophotometric assay of DOM in pharmaceuticals [27] in which four procedures are described. The first two methods are based on redox-complexation reactions involving Fe^{3+}, *o*-phenanthroline and bipyridyl [27] and the other two methods utilized cerium(IV) as the oxidimetric reagent, which was subsequently determined by decrease of red color of chromotrope 2R or orange pink color of Rhodamine 6G [27].

The reported four visible spectrophotometric methods [27] involve a heating step and the procedures based on redox-complexation reactions require strict pH control. The present communication reports three simple and sensitive spectrophotometric methods for the assay of DOM in bulk drug and in tablets based on bromination of DOM by *in situ* generated bromine. The proposed methods have the advantages of speed, free from stringent experimental conditions like heating step and pH adjustment, besides being accurate and precise. In addition to these, the highlight of the present investigation is the use of cheap and eco-friendly green brominating agent i.e. bromate-bromide mixture and avoidance of corrosive liquid bromine. This is one step towards green chemistry.

EXPERIMENTAL DETAILS

Apparatus. All absorbance measurements were made on a Systronics model 106 digital spectrophotometer (Ahmedabad, India) provided with 1-cm matched quartz cells.

Materials and reagents. All chemicals and reagents used were of analytical or pharmaceutical grade. Distilled water was used to prepare the solutions.

Bromate-bromide mixture (200, 40 and 12 μg mL^{-1}). A stock standard solution of bromate-bromide mixture equivalent to 1000 μg mL^{-1} $KBrO_3$ containing an excess KBr was prepared by dissolving accurately weighed 100 mg of $KBrO_3$ (S. D. Fine Chem. Ltd., Mumbai, India) and 1 g of KBr (Merck, Mumbai, India) in water and diluting to 100 mL in a calibrated flask. The stock solution was diluted stepwise to obtain 40, 200 and 12 μg mL^{-1} solutions with respect to $KBrO_3$ for use in methods A, B and C, respectively.

Meta cresol purple solution (80 μg mL^{-1}). A 400 μg mL^{-1} stock solution was first prepared by dissolving 40 mg of dye (Loba Chemie, Mumbai, India) in 2 mL of 0.1 N NaOH and diluted to volume with water in a 100 mL calibrated flask, and was diluted further to get a working concentration of 80 μg mL^{-1} dye solution.

Amaranth solution (200 μg mL^{-1}). The solution was prepared by dissolving 24 mg of dye (S. D. Fine Chem. Ltd., Mumbai, India; dye content 85%) in water and diluting to 100 mL with water in a calibrated flask.

Erioglaucine solution (200 μg mL^{-1}). The solution was prepared by dissolving 20 mg of dye (Loba Chemie, Mumbai, India) in water and diluting to 100 mL with water in a calibrated flask.

Hydrochloric acids (10, 5, 2 and 1 M). The solutions were prepared by appropriate dilution of concentrated acid (S. D. Fine Chem. Ltd., Mumbai, India; Sp. gr. 1.18) with water.

Standard DOM solution. Pharmaceutical grade DOM certified to be 99.85% was kindly provided by Cipla India Ltd., Mumbai, India, and was used as received. A stock standard solution of 500 μg mL^{-1} DOM was first prepared by dissolving 50 mg of pure drug in 100 mL of 3:7 dilute acetic acid (acetic acid:water), and was further diluted stepwise with the same acid to get 25, 10 and 5 μg mL^{-1} DOM for methods A, B and C, respectively.

Two brands of tablets containing DOM, Domstal-10 (Torrent Pharmaceuticals Ltd., M.P., India) and Vemistop-10 (Cipla Ltd., H.P., India) used in the investigation were purchased from local commercial sources.

Sample preparation

Tablets. Ten tablets were accurately weighed and powdered. A portion equivalent to 25 mg was transferred into a 50 mL calibrated flask, 30 mL of 3:7 dilute acetic acid (acetic acid:water) was added to the flask and the content was shaken thoroughly for 15-20 min to extract the drug into the liquid phase; the volume was finally diluted to the mark with the same acid (50 mL flask), mixed well and filtered using a Whatman No. 42 filter paper. The filtrate equivalent to 500 μg mL^{-1} was further diluted with the same acid to get 25, 10 and 5 μg mL^{-1} for methods A, B and C, respectively.

Placebo blank. A placebo blank of the composition: talc (43 mg), starch (35 mg), acacia (25 mg), methyl cellulose (40 mg), sodium citrate (25 mg), magnesium stearate (35 mg) and sodium alginate (30 mg) was made and its solution was prepared in 25 mL calibration flask as described under “Procedure for tablets“.

Synthetic mixture. To the placebo blank of the composition described above, 25 mg of DOM was added and homogenized, transferred to a 50 mL calibrated flask and the solution was prepared as described under “Procedure for tablets”.

General procedures

Method A (using MCP). Different aliquots (0.25, 0.5, 1.0, 2.0, 3.0 and 4.0 mL) of 25 μg mL^{-1} DOM solution were accurately transferred into a series of 10 mL calibrated flasks using micro burette and the total volume was adjusted to 4.0 mL by adding 3:7 acetic acid. To each flask were added 1 mL each of 10 M HCl and bromate-bromide (40 μg mL^{-1} w.r.t $KBrO_3$). The flasks were stoppered, the content was mixed well and the flasks were let to stand for 15 min with occasional shaking. Then, 1 mL of 80 μg mL^{-1} MCP was added to each flask by means of micro burette, diluted to the mark with water, mixed and absorbance of each solution was measured at 530 nm against a reagent blank.

Method B (using AMR). Varying aliquots (0.25, 0.5, 1.0, 2.0, 3.0 and 4.0 mL) of DOM solution (10 μg/mL^{-1}) were accurately measured into a series of 10 mL calibrated flasks by means of micro burette and the total volume was brought to 4 mL by adding 3:7 acetic acid. To each flask were added 1 mL of 5M HCl followed by 1 mL of $KBrO_3$-KBr solution (200 μg mL^{-1} w.r.t. $KBrO_3$). The flasks were stoppered immediately, content mixed, and kept aside for 10 min with occasional shaking. Lastly, 1 mL of 200 μg mL^{-1} AMR solution was added to each flask and diluting up to the mark with water. The absorbance of each solution was measured at 520 nm against reagent blank.

Method C (using EGC). Different aliquots (0.25, 0.5, 1.0, 2.0, 3.0 and 4.0 mL) of standard DOM solution (5 μg mL^{-1}) were transferred into a series of 10 mL standard calibrated flasks and the total volume in each flask was adjusted to 4 mL with 3:7 acetic acid. Added to each flask were 1 mL of 1 M HCl and 1 mL of bromate-bromide (12 μg mL^{-1} w.r.t $KBrO_3$). The flasks were stoppered, the content was mixed and the flasks were let stand for 10 min with occasional shaking. Then, 1 mL of 2 M HCl and 1 mL 200 μg mL^{-1} EGC were added to each flask by means of micro burette, diluted to the mark with water, mixed and absorbance of each solution was measured at 630 nm against a reagent blank after 5 min.

RESULTS AND DISCUSSION

The bromate-bromide mixture with a number of dyes like methyl orange, indigo carmine, methylene blue, rhodamine-B, meta cresol purple etc. has successfully been employed for the assay of several pharmaceuticals [28-31]. From the preliminary experiments, DOM was found to undergo bromination by bromine, generated *in situ* by the action of acid on bromate-bromide mixture and the dyes, meta cresol purple, amaranth and erioglaucine were found to undergo bleaching in acid medium by bromine. Based on this observation, three indirect spectrophotometric methods using bromate-bromide mixture and three dyes, meta-cresol purple (MCP), amaranth (AMR) and erioglaucine (EGC) were developed. The proposed methods are based on the bromination of DOM by a measured excess of *in situ* bromine followed by the determination of the residual bromine by reacting it with the cited dyes. The amount of bromine reacted corresponds to the amount of drug initially present. The pink color of MCP and AMR in acid medium exhibited strong absorbtion maxima at 530 and 520 nm, respectively, and the green color of EGC dye in acid medium absorbs maximally at 630 nm (Figure 2).

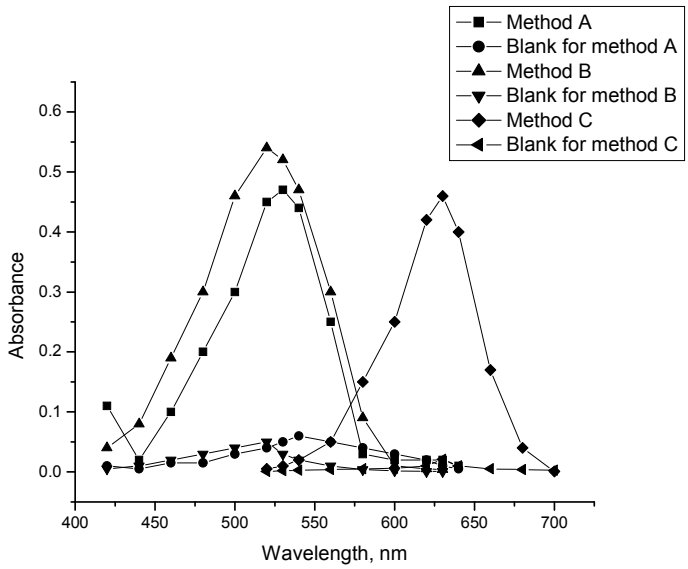

Figure 2. Absorption spectra (5 μg mL^{-1} DOM in method A, 3 μg mL^{-1} DOM in method B and 1 μg mL^{-1} DOM in method C).

DOM when added in increasing concentrations to a fixed concentration of *in situ* generated bromine, consumes the latter proportionately and there occurs a concomitant fall in the concentration of bromine. When a fixed concentration of either dye was added to the decreasing concentrations of bromine, a concomitant increase in the concentration of dye resulted. This was observed as a proportional increase in the absorbance at the respective λ_{max} with increasing concentration of DOM.

Chemistry

Since DOM contains aromatic amines, it undergoes an electrophilic aromatic substitution reaction with *in situ* generated bromine. Nitrogen atoms attached to the benzene ring are *ortho*- and *para*-directors [32] but the bromination of DOM occurs at the *para*-positions only due to the steric effect of the amide which leads to a decrease in the amount of the *ortho*-product.

Hydroxy substituents activate the benzene ring and direct the electrophile towards *ortho*- and *para*-positions, whereas the sulphonate substituent deactivates the benzene ring and directs the electrophile towards *meta*-position [32]. Hence, bromination of the dyes, *meta* cresol purple (MCP), amaranth (AMR) and erioglaucine (EGC) with the unreacted bromine occurs either at *ortho*- and *para*- positions to the -OH groups or *meta* to the sulphonate group or *ortho*- and *para*- to the nitrogen atom. In all the methods, bleaching occurs because of the bromination of the dyes. The probable reaction mechanisms are shown in Figure 3.

Optimization of variables

Preliminary experiments were performed to determine the concentration of each dye; producing a reasonably high absorbance; and these were found to be 8, 20 and 20 μg mL^{-1} for MCP, AMR and EGC, respectively. The $KBrO_3$ concentration (in the presence of excess KBr) required to bleach the dyes completely in acid medium was also determined and found to be 4 μg mL^{-1} for MCP, 20 μg mL^{-1} for AMR and 1.2 μg mL^{-1} for EGC. Hence, different concentrations of DOM were reacted with 1.0 mL each of 40 μg mL^{-1} $KBrO_3$ in method A, 200 μg mL^{-1} $KBrO_3$ in method B and 12 μg mL^{-1} $KBrO_3$ in method C, before determining the residual bromine as described under the respective procedures. Hydrochloric acid was the ideal medium for bromination reaction as well as the determination of residual bromine by using any of the studied dyes. In method A, the reaction between DOM and bromine (*in situ*) was unaffected when 1.5-3.0 mL of 5 M HCl was used (Figure 4). Hence, 1 mL of 10 M HCl equivalent to 2 mL of 5 M HCl was used for both steps of the reaction. In method B, since (0.5-3.0) mL of 5 M HCl gave constant absorbance readings (Figure 4), 1 mL of 5 M HCl was used for both steps of the reaction. However, in method C, bromination of DOM was found to be faster in lower acid concentration and bleaching of EGC by bromine required higher concentration of acid. For the bromination step, 1 mL of 1 M HCl was used, since (0.5-2.0) mL of 1 M HCl gave constant absorbance readings (Figure 5), and for the bleaching step further addition of 1 mL of 2 M HCl was necessary. At lower acid concentrations, bleaching of dye took a longer time. For quantitative reaction between DOM and bromine (*in situ*), a contact time of 15 min was found sufficient in method A and 10 min in both methods B and C and constant absorbance readings were obtained when contact times were extended up to 30 min in all the methods (Figure 6). The bleaching of the dyes was found to be instantaneous in methods A and B, while 5 min was required in method C.

Method validation

The proposed methods have been validated for linearity, sensitivity, precision, accuracy, robustness, ruggedness, selectivity and recovery according to the International Conference on Harmonization (ICH) [33] guidelines.

Linearity and sensitivity. Under optimum conditions a linear relation was obtained between absorbance and concentration of DOM in the range of 0.63--10.0 μg mL^{-1} (method A), 0.25-4.0 μg mL^{-1} (method B) and 0.13-2.0 μg mL^{-1} (method C). The linear plots gave the following regression equations:

$y = 0.010 + 0.086x$ for method A,
$y = 0.020 + 0.164x$ for method B and
$y = 0.008 + 0.452x$ for method C

where y = absorbance and x = concentration in μg mL^{-1}) obtained by the method of least squares. The correlation coefficient, intercept and slope for the calibration data are summarized in Table 1. Sensitivity parameters such as apparent molar absorptivity and sandell sensitivity values, the limit of detection (*LOD*) and the limit of quantification (*LOQ*) are calculated as per the current ICH guidelines [33] are compiled in Table 1 speak of the excellent sensitivity of the proposed method. *LOD* and *LOQ* were calculated according to the same guidelines using the formulae:

$LOD = 3.3\sigma/s$ *and* $LOQ = 10\sigma/s$

where σ is the standard deviation of five reagent blank determinations and s is the slope of the calibration curve.

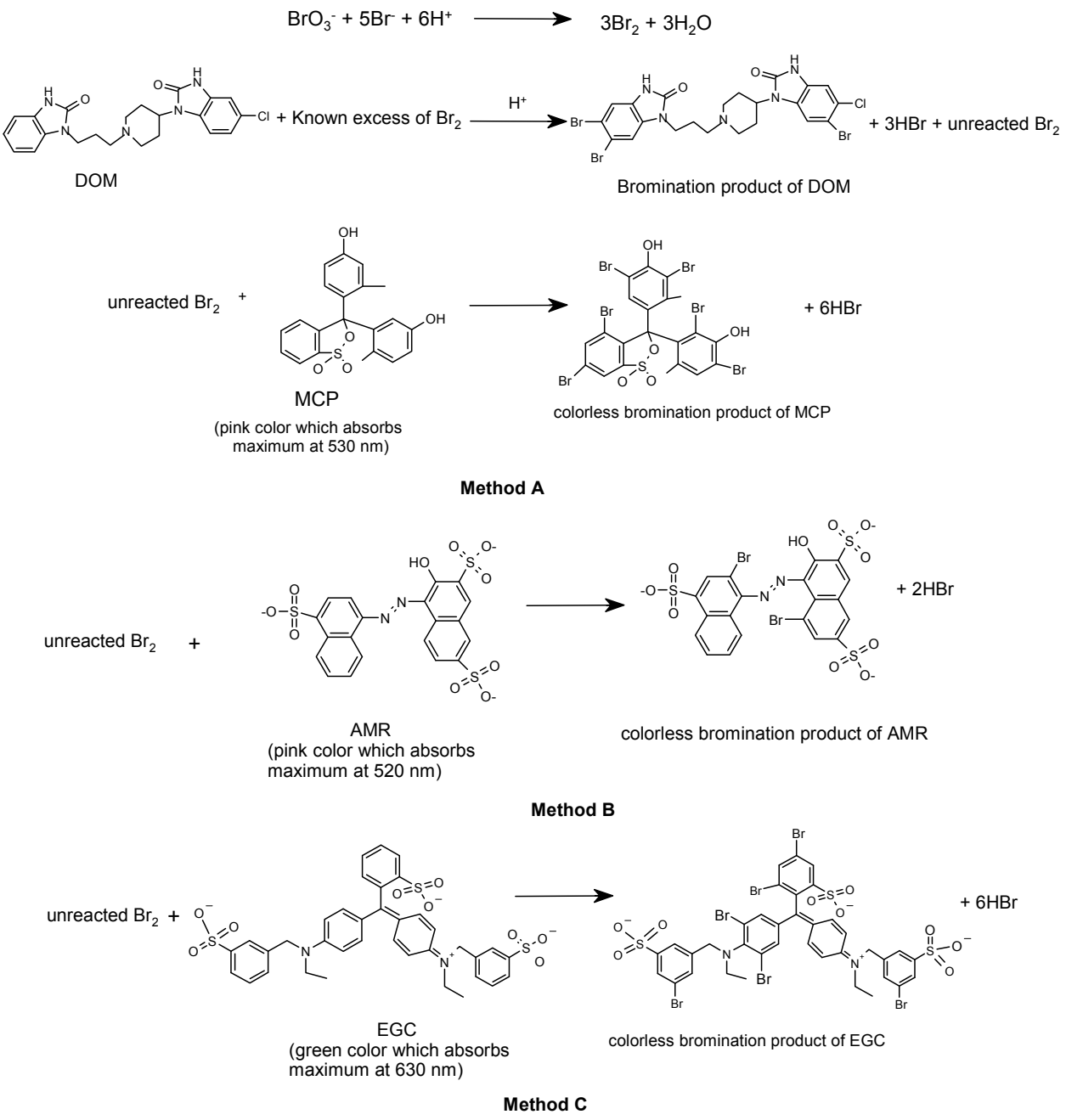

Figure 3. Probable reaction scheme.

Precision and accuracy. Intra-day precision and accuracy of the proposed methods were evaluated by replicate analysis (n = 7) of calibration standards at three different concentration levels in the same day. Inter-day precision and accuracy were determined by assaying the calibration standards at the same concentration levels on five consecutive days. Precision and accuracy were based on the calculated relative standard deviation (*RSD* / %) and relative error (*RE* / %) of the found concentration compared to the theoretical one, respectively (Table 2).

Robustness and ruggedness. Method robustness was tested by making small incremental change in HCl concentration and reaction time in all the methods. To check the ruggedness, analysis was performed by four different analysts, and on three different spectrophotometers by the same analyst. The robustness and the ruggedness were checked at three different drug levels. The intermediate precision, expressed as percent RSD, which is a measure of robustness and ruggedness was within the acceptable limits as shown in Table 3.

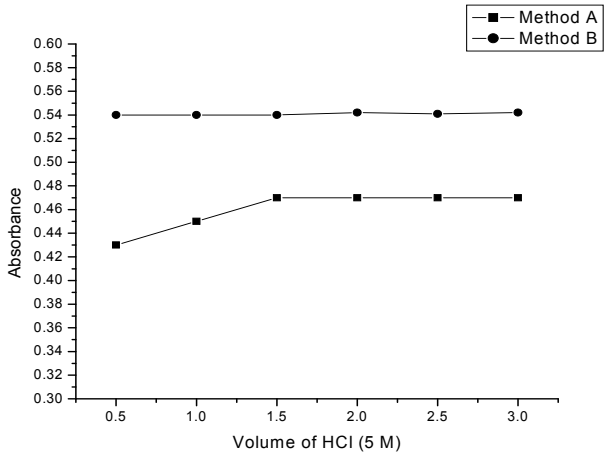

Figure 4. Effect of HCL in methods A and B (5 μg mL^{-1} DOM in method A and 3 μg mL^{-1} DOM in method B).

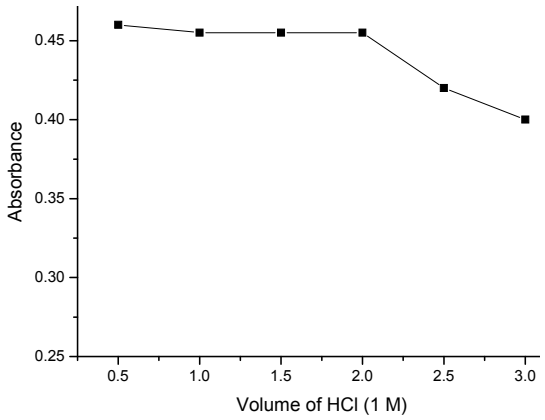

Figure 5. Effect of HCL (1 μg mL^{-1} DOM) in method C.

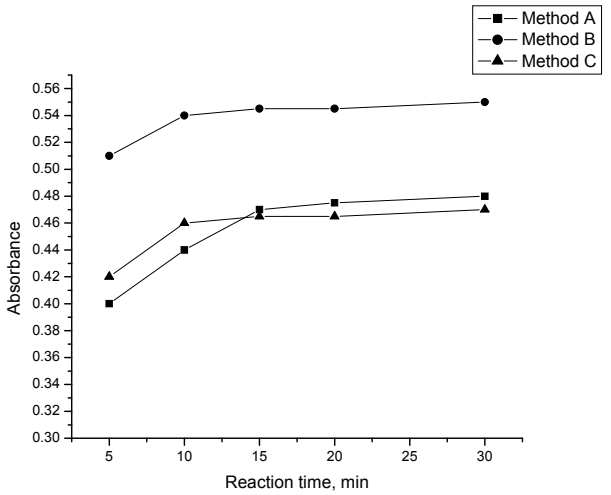

Figure 6. Effect of reaction time (5 μg mL^{-1} DOM in method A, 3 μg mL^{-1} DOM in method B and 1 μg mL^{-1} DOM in method C).

Selectivity. The proposed methods were tested for selectivity by placebo blank and synthetic mixture analyses. A convenient aliquot of the placebo blank solution was subjected to analysis according to the recommended procedures. In all the cases, there was no interference by the inactive ingredients.

Table 1. Sensitivity and regression parameters

Parameter	Method		
	A	B	C
λ_{max} / nm	530	520	630
Linear range, μg mL^{-1}	0.63-10.0	0.25-4.0	0.13-2.0
Molar absorptivity (ε), L mol^{-1} cm^{-1}	3.75×10^4	6.60×10^4	1.99×10^5
Sandell sensitivity[a], μg cm^{-2}	0.011	0.006	0.002
LOD / μg mL^{-1}	0.07	0.04	0.00
LOQ / μg mL^{-1}	0.21	0.13	0.01
Regression equation, *y*[b]			
Intercept (*a*)	0.010	0.020	0.008
Slope (*b*)	0.086	0.164	0.452
Standard deviation of *a* (S_a)	0.047	0.126	0.037
Standard deviation of *b* (S_b)	0.005	0.036	0.020
Regression coefficient (*r*)	0.997	0.997	0.999

[a]Limit of determination as the weight in μg per mL of solution, which corresponds to an absorbance of $A = 0.001$ measured in a cuvette of cross-sectional area 1 cm^2 and $l = 1$ cm; [b]$y = a + bX$, Where y is the absorbance, x is concentration in μg mL^{-1}, a is intercept, b is slope

A separate experiment was performed with the synthetic mixture. The analysis of synthetic mixture solution yielded percent recoveries which ranged 97.58-104.3% with standard deviation of 1.62-2.41% in all the cases. The results of this study, presented in Table 4, indicate that the inactive ingredients did not interfere in the assay. These results further demonstrate the accuracy as well as the precision of the proposed methods.

Application to assay in tablets

In order to evaluate the analytical applicability of the proposed methods to the quantification of DOM in commercial tablets, the results obtained by the proposed methods were compared to those of the reference method [3] by applying Student's *t*-test for accuracy and *F*-test for precision. The results (Table 5) show that the Student's *t*- and *F*-values at 95% confidence level are less than the theoretical values, which confirmed that there is a good agreement between the results obtained by the proposed methods and the reference method with respect to accuracy and precision.

Recovery studies. The accuracy and validity of the proposed methods were further ascertained by performing recovery studies. Pre-analysed tablet powder was spiked with pure DOM at three concentration levels (50, 100 and 150% of that in tablet powder) and the total was found by the proposed methods. In all cases, the added DOM recovery percentage values

Table 2. Evaluation of intra-day and inter-day accuracy and precision (RE: relative error; RSD: relative standard deviation)

Method	DOM taken μg mL^{-1}	Intra-day accuracy and precision (n = 7)			Inter-day accuracy and precision (n = 7)		
		DOM found, μg mL^{-1}	*RE* / %	*RSD* / %	DOM found, μg mL^{-1}	*RE* / %	*RSD* / %
Method A (using MCP)	2.5	2.44	2.40	2.41	2.43	2.80	2.37
	5.0	5.13	2.61	2.27	5.15	3.00	2.31
	7.5	7.68	2.46	1.21	7.71	2.80	2.05
Method B (using AMR)	2.0	1.96	2.00	0.57	1.94	3.00	3.13
	3.0	3.05	1.67	1.76	2.93	2.33	2.97
	4.0	3.90	2.50	0.89	4.11	2.75	3.19
Method C (using EGC)	0.5	0.486	2.80	2.07	0.485	3.00	2.11
	1.0	1.02	2.00	1.41	0.971	2.87	2.78
	1.5	1.54	2.67	1.93	1.459	2.73	2.16

Table 3. Robustness and ruggedness expressed as intermediate precision (%RSD)

Method	DOM taken μg mL^{-1}	Method robustness		Method ruggedness	
		Parameter altered			
		HCl, mL[a]; *RSD*[b], % () (n = 3)	Reaction time[c], min; RSD, % (n = 3)	Inter-analysists' *RSD*, % (n = 4)	Inter-instruments' *RSD*, % (n = 3)
Method A (using MCP)	2.5	1.57	2.07	1.18	3.36
	5.0	1.35	1.68	1.09	3.29
	7.5	1.43	1.74	1.02	3.32
Method B (using AMR)	2.0	1.23	1.64	1.06	2.41
	3.0	1.19	1.41	0.97	2.26
	4.0	1.31	1.95	1.12	2.35
Method C (using EGC)	0.5	1.25	1.32	1.01	3.39
	1.0	1.16	1.27	1.13	4.28
	1.5	1.19	1.25	1.05	4.31

[a]HCl volumes used were 0.8, 1.0 and 1.2 mL in all the three methods; [b]10 M in method A, 5 M in method B and 1 M in method C; [c]reaction times altered were 13, 15 and 17 min in method A and 8, 10 and 12 min in both methods B and C

Table 4. Recovery of the drug from synthetic mixture

Method	DOM in synthetic mixture taken, μg mL^{-1}	DOM recoverd[a]±*SD*, %
Method A (using MCP)	2.5	102.5±2.27
	5.0	104.3±1.77
	7.5	103.2±2.41
Method B (using AMR)	1.0	98.50±1.62
	2.0	97.58±1.84
	3.0	99.21±2.10
Method C (using EGC)	0.5	102.9±1.93
	1.0	103.1±1.64
	1.5	102.4±1.87

[a]Mean value of five determinations

ranged 105.56-112.3% with standard deviation of 1.51-2.14% (Table 6) indicating that the recovery was good, and that the co formulated substance did not interfere in the determination.

CONCLUSIONS

Three rapid, relatively specific, accurate and precise spectrophotometric methods for the determination of DOM in pure form and in tablets were developed and validated as per as the current ICH guidelines. Compared with most of the existing methods for DOM, the present methods are very simple and cost effective. Of the non-chromatographic methods, the methods based on voltammetric [4,5] and potentiometric sensor [6] techniques involve rigid pH control. The chromatographic techniques [7-25] although

Table 5. Results of analysis of tablets by the proposed methods

Tablet brand name	Label claim mg/tablet	Found[a]±*SD*, % (percent of label claim, *n* = 5)			
		Reference method	Method A (using MCP)	Method B (using AMR)	Method C (using EGC)
Domstal-10[b]	10	102.47±1.54	104.5±1.74 *t* = 1.95 *F* = 1.27	105.2±1.71 *t* = 2.65 *F* = 1.23	103.5±1.58 *t* = 1.04 *F* = 1.05
Vomistop-10[c]	10	100.3±1.52	101.3±1.54 *t* = 1.03 *F* = 1.21	103.0±1.84 *t* = 2.44 *F* = 1.47	102.5 ± 1.61 *t* = 2.22 *F* = 1.12

[a]Mean value of five determinations; [b]Torrent Pharmaceuticals Ltd., M. P, India; [c]Cipla Ltd., H. P., India. The value of t (tabulated) at 95 % confidence level and for four degrees of freedom is 2.77. The value of F (tabulated) at 95 % confidence level and for four degrees of freedom is 6.39

Table 6. Accuracy assessment by recovery experiment

Method	Tablet studied	DOM in tablet μg mL^{-1}	Pure DOM added μg mL^{-1}	Total found μg mL^{-1}	Pure DOM recovered[a]±*SD* %
Method A (using MCP)	Vemistop-10	2.53	1.25	3.85	105.56±1.51
		2.53	2.5	5.21	107.27±2.01
		2.53	3.75	6.69	110.93±2.06
Method B (using AMR)		1.03	0.5	1.59	112.0±1.64
		1.03	1.0	2.12	109.0±1.86
		1.03	1.5	2.64	107.3±2.08
Method C (using EGC)		0.51	0.25	0.786	110.4±1.99
		0.51	0.5	1.05	107.9±2.14
		0.51	0.75	1.35	112.3±1.73

[a]Mean value of five determinations

sensitive, require expensive instrumental-set up. A large volume of solvents is required for these techniques, which are expensive, hazardous to health, and harmful to the environment. HPLC requires precolumn derivatization without preliminary separation. It requires either an organic solvent extraction or use of surfactants and alcohols in the mobile phase. The reported four visible spectrophotometric methods [27] require boiling for 5-10 min and in addition to this, the procedures based on redox-complexation reaction also require strict pH control.

In contrast to the above published methods, the present methods are free from unwelcome steps such as heating or extraction and also from critical pH conditions. The methods are also useful due to high tolerance limit for common excipients found in drug formulations. These merits coupled with the use of simple and eco-friendly green brominating agent and avoidance of use of corrosive liquid bromine, the present investigation represents relatively green procedures.

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O. ZENITA DEVI
K. BASAVAIAH
K.B. VINAY

Department of Chemistry, University of Mysore, Manasagangotri, Mysore, India

NAUČNI RAD

SPEKTROFOTOMETRIJSKO ODREĐIVANJE DOMPERIDONA U FARMACEUTSKIM PREPARATIMA PRIMENOM REAKCIJE OKSIDACIJE BROMATA

U radu su opisane tri jednostavne i osetljive spektrofotometrijske metode za određivanje domperidona (DOM), u rasutom stanju i u formi lekova korišćenjem smeše bromata i brimida, kao reagensa za bromovanje u kiseloj sredini, i tri boje, ljubičasti meta-krezol (MCP), amarant (AMR) i erioglaucin (EGC). Metode se zasnivaju na dodavanju poznatog viška smeše bromata i bromida zakišeljenom rastvoru DOM-a i određivanju rezidualnog broma reakcijom sa određenom količinom boje. Talasne dužina određivanja sa bojama MCP (metoda A), AMR (metoda B) i EGC (metoda C) su 530, 520 i 630 nm, respektivno. Odeđivanja su u skladu sa Beer-ovim zakonom u opsegu koncentracijska od 0,63-10,0, 0,25-4,0 i 0,13-2,0 μg mL^{-1} za metode A, B i C, redom. Izračunate molarne apsorptivnosti iznose: 3.751×10^4, 6.604×10^4 and 1.987×10^5 L mol^{-1} cm^{-1} za metode A, B i C, redom, a odgovarajući Sandell-ovi indeksi su: 0,011, 0,006 i 0,002 μg cm^{-2}. Limiti detekcije i limiti kvantifikacije su, takođe, određeni za sve tri metode. Nije zapažena interferencija sa uobićajenim aditivima koji se nalaze u farmaceutskim preparatima. Statistička poređenja rezultata sa onima u referentnoj metodi pokazala su odlična slaganja, što je ukazalo da nema značajne razlike u tačnosti i preciznosti između metoda. Tačnost i pouzdanost metode su dodatno potvrđeni određivanjem procenta prinosa (recovery vrednosti) metodom standardnog dodataka.

Ključne reči: domperidon; određivanje; spektrofotometrija; bromat-bromid; boje; tablete.