

## Spectral resolution and simultaneous determination of oxymetazoline hydrochloride and sodium cromoglycate by derivative and ratio-based spectrophotometric methods

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### ARTICLE INFORMATION



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### ABSTRACT

Sodium cromoglycate (SCG) and oxymetazoline hydrochloride (OXMT) are administered in combination for effective treatment of nasal congestion and allergy. In this work, SCG was determined using direct spectrophotometry by measuring its zero order absorption spectra at its  $\lambda_{\max}$  320.6 nm where OXMT showed zero absorbance. On the other hand, four simple, sensitive and precise spectrophotometric methods were developed and validated for the determination of OXMT in the presence of SCG in their laboratory prepared mixtures and pharmaceutical formulation, without preliminary separation; Method A: first derivative spectrophotometric method [1D], Method B: first derivative of ratio spectra method [1DD], Method C: ratio difference spectrophotometric method [RDSM] and Method D: ratio subtraction method [RSM]. Ratio manipulating methods (Method B, C and D) were done using divisor of 10.00  $\mu\text{g/mL}$  SCG. Linear correlation was obtained in range 4-22  $\mu\text{g/mL}$  for OXMT by methods A, B and D and 6-22  $\mu\text{g/mL}$  for method C. All methods were validated in compliance with the International Conference on Harmonization (ICH) guidelines and satisfactory results were obtained. No significant difference was noted between the developed methods and the official one with respect to accuracy and precision.

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### 1. Introduction

Chemically, sodium cromoglycate is 5,5'-(2-hydroxy propane-1,3-diyl)bis(oxy)bis(4-oxo-4H-chromene-2-carboxylic acid) disodium salt (Figure 1a). It exerts its action via preventing the release of mediators that would normally attract inflammatory cells [1]. Oxymetazoline hydrochloride is chemically designated as 3-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2,4-dimethyl-6-tert-setyl-phenol hydrochloride salt (Figure 1b). It is a sympathomimetic agent that selectively acts on  $\alpha_1$  and partially on  $\alpha_2$  adrenergic receptors [2]. Both drugs are co-formulated in a nasal spray dosage form and are widely used for effective treatment of nasal congestion and allergy. Several methods have been reported for the determination of SCG in pharmaceutical preparations such as spectrophotometry [3,4], electrophoresis [5], electrochemical [6,7] and HPLC methods [8-14]. OXMT has also been analyzed by several methods in pharmaceutical preparations such as spectrophotometry [3,15-23], capillary electrophoresis [24,25], gas chromatography [26,27] and HPLC [28-35].

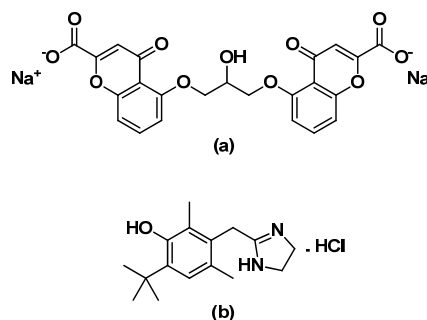


Figure 1. Chemical structures of (a) sodium cromoglycate (SCG) and (b) oxymetazoline hydrochloride (OXMT).

To the best of our knowledge, Abdel-Aziz *et al.* [3] developed new accurate, sensitive and selective spectrophotometric and spectrofluorimetric methods for determination of SCG and OXMT. The aim of this study is to develop simple, accurate, precise and time saving spectrophotometric methods

for the routine analysis of SCG and OXMT in quality control laboratories either in their pure forms or in pharmaceutical formulations with no prior separation.

## 2. Experimental

### 2.1. Instrumentation

A Shimadzu dual beam UV-visible spectrophotometer, model 1601 PC connected to an IBM compatible personal computer and the bundled software, UV-PC personal spectroscopy software version (3.7) were used in all determinations (Shimadzu, Kyoto, Japan). The spectral band width was 0.2 nm with wavelength scanning speed of 2800 nm/min.

### 2.2. Pure samples and pharmaceutical formulations

SCG pure sample was supplied by SIGMA Pharmaceutical industries, Egypt. Pure sample of OXMT was supplied by National Organization for Drug Control and Research (NODCAR), Egypt. Their purity were checked and found to be  $101.5 \pm 1.01$  and  $99.93 \pm 1.01$  for SCG and OXMT, respectively, according to the USP reference methods [36] which are spectrophotometric and HPLC methods for SCG and OXMT, respectively. Nasocrom® nasal spray (SIGMA Pharmaceutical industries, Egypt), labeled to contain 2g of SCG and 0.025g of OXMT per 100 mL (Batch number: 11087) was obtained from the local market.

### 2.3. Standard solutions and laboratory prepared mixtures

Stock standard solutions of SCG and OXMT (1.00 mg/mL) were prepared by dissolving 100 mg of each drug in 100 mL methanol. Working standard solutions of SCG and OXMT (0.10 mg/mL) were prepared by diluting 10 mL from their respective stock standard solutions (1.00 mg/mL) into two separate 100-mL volumetric flasks and the volume was completed with methanol. Into a series of 10 mL volumetric flasks, aliquots of SCG and OXMT were accurately transferred from their corresponding working solutions and then the volumes were completed to the mark with methanol in order to prepare mixtures containing different ratios of the two drugs.

## 2.4. Procedures

### 2.4.1. Spectral characteristics of SCG and OXMT

The absorption spectrum of 10.00 µg/mL of each of SCG and OXMT solutions were recorded in the wavelength range 200-400 nm against methanol as a blank.

### 2.4.2. Construction of calibration curves

SCG: Aliquots equivalent to 10.00-250.00 µg of SCG were accurately transferred from its working standard solution (0.10 mg/mL) into a series of 10 mL volumetric flasks then the volumes were completed to the mark with methanol. The absorption spectra of the prepared solutions were recorded against methanol as a blank (200-400 nm) the values of absorbance of SCG at its  $\lambda_{\max}$  (320.6 nm) were plotted against their corresponding concentrations (1.00-25.00 µg/mL) and the regression parameters were computed.

OXMT: Aliquots equivalent to 10.00-250.00 µg OXMT were accurately transferred from its working standard solution (0.10 mg/mL) into a series of 10 mL volumetric flasks then the volumes were completed to the mark with methanol. The absorption spectra of the prepared solutions of OXMT were recorded against a blank of methanol and stored for subsequent manipulation.

### 2.4.3. Method A: First derivative spectrophotometric method [<sup>1</sup>D]

The first derivative (<sup>1</sup>D) of the scanned OXMT spectra was calculated ( $\Delta\lambda = 8$ , scaling factor =10). A calibration curve representing the relation between the amplitude of <sup>1</sup>D at 289.2 nm to the corresponding concentrations (4.00-22.00 µg/mL) was constructed and the regression equation was computed.

### 2.4.4. Method B: First derivative of ratio spectra method [<sup>1</sup>DD]

The stored scanned spectra of OXMT (1.00-25.00 µg/mL) were divided by a standard spectrum of SCG (10.00 µg/mL) and <sup>1</sup>DD was then obtained ( $\Delta\lambda = 8$ , scaling factor =1.0). A calibration curve representing the relation between peak amplitude of <sup>1</sup>DD at 292 nm to the corresponding concentrations (6.00-22.00 µg/mL) was constructed and the regression equation was computed.

### 2.4.5. Method C: Ratio difference method (RD)

The stored scanned spectra of OXMT (1.00-25.00 µg/mL) were divided by a standard spectrum of SCG (10.00 µg/mL) and the amplitude of the ratio spectra at 286.6 and 294.0 nm were recorded. A calibration curves was constructed by plotting the difference between the amplitude ratio difference ( $\Delta P$  286.6-294 nm) versus the corresponding concentrations (4.00-22.00 µg/mL) and the regression equations were computed.

### 2.4.6. Method D: Ratio subtraction method (RS)

A calibration curve representing the relation between absorbance of OXMT at  $\lambda_{\max} = 282.6$  nm to the corresponding concentrations (4.00-22.00 µg/mL) was constructed and the regression equation was computed.

### 2.4.7. Analysis of laboratory prepared mixtures

The absorption spectra of laboratory prepared mixtures were recorded and the procedures were performed as described. The concentrations of SCG and OXMT were calculated using the corresponding regression equations.

### 2.4.8. Application to Nasocrom® nasal spray and standard addition

Aliquots of 0.5 mL of Nasocrom nasal spray was mixed with 2.38 mg OXMT then transferred into 100 mL volumetric flask, the volume was completed with methanol to get 100.00 µg/mL of SCG and 25.00 µg/mL of OXMT, and the prepared solution was filtered through 0.45 µm membrane filter. An appropriate dilution was made with methanol to prepare the working solution containing 10.00 µg/mL of SCG and 2.50 µg/mL of OXMT. Three replicates for each experiment were done. The concentrations of pure SCG and OXMT were calculated from their corresponding regression equations. When carrying out the standard addition technique, different known concentrations of pure standard SCG and OXMT were added to the pharmaceutical formulation before proceeding in the previously mentioned methods.

## 3. Results and discussion

The aim of this work was to develop simple, sensitive, selective and precise spectrophotometric methods for simultaneous determination of binary mixture of SCG and OXMT in their pure form and pharmaceutical formulation. The absorption spectra of SCG and OXMT showed a severe overlap in the region 200-300 nm, while from 300-400 nm OXMT had

no spectral contribution. This allowed the determination of SCG at  $\lambda_{\max} = 320.6$  nm without any interference from OXMT, as shown in Figure 2. However, SCG interfere with the determination of OXMT which necessitates the application of spectral manipulation for its determination through removing the interference of SCG.

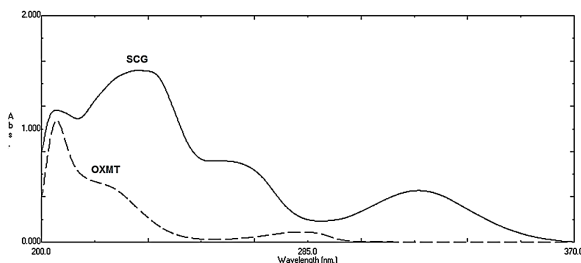


Figure 2. Zero-order spectra of sodium cromoglycate (—) and oxymetazoline hydrochloride (---) in methanol, 10.00 µg/mL each.

### 3.1. Determination of SCG using direct spectrophotometry

A linear relationship was obtained between absorbance of SCG at 320.6 nm and the corresponding concentration in the range of (1.00-25.00 µg/mL). The linear regression equation was found to be:

$$A = 0.0454C + 0.0056 \quad r = 1.0000 \quad (1)$$

where A is the absorbance at 320.6 nm, C is the concentration and r is the correlation coefficient.

### 3.2. Determination of OXMT

#### 3.2.1. Method A: First derivative spectrophotometric method [D1]

Figure 3 showed the <sup>1</sup>D spectra for the two drugs, where OXMT exhibited peak maxima at 289.2 nm, while SCG did not interfere. The wavelength increment over which the derivative was obtained ( $\Delta\lambda$ ) was carefully tested,  $\Delta\lambda = 8$  and scaling factor of 10 gave a suitable signal to noise ratio and the spectra showed good resolution. A linear relationship was obtained between peak amplitude at the selected wavelength and the corresponding concentration in the range of (4.00-22.00 µg/mL). The linear regression equation was found to be:

$$P = 0.0068C + 0.0007 \quad r = 0.9994 \quad (2)$$

where P is the <sup>1</sup>D peak amplitude at 289.2 nm, C is the concentration and r is the correlation coefficient.

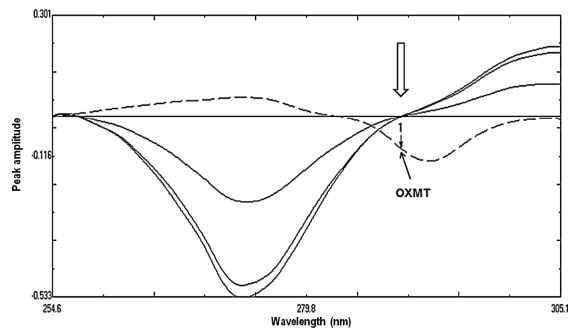


Figure 3. First derivative spectra <sup>1</sup>D of 5.00 µg/mL of oxymetazoline hydrochloride (—) and three different concentrations (5.00, 10.00 and 15.00 µg/mL) of sodium cromoglycate (---).

#### 3.2.2. Method B: First derivative of ratio spectra method [1DD]

Figure 4 shows the <sup>1</sup>DD spectra using SCG (10.00 µg/mL) as a divisor, where OXMT shows a peak maxima at 292 nm with no interference of SCG and the whole spectrum of the interfering substance is cancelled. Accordingly, the choice of the wavelength selected for calibration is not critical as in the <sup>1</sup>D method. The ratio spectra for OXMT (6.00-22.00 µg/mL) were obtained and then <sup>1</sup>DD spectra were calculated. A linear relationship was obtained between peak amplitude at  $\lambda = 292$  nm and the corresponding concentration in the range of 6.00-22.00 µg/mL. The linear regression equation was found to be:

$$P = 0.0525C - 0.0028 \quad r = 0.9999 \quad (3)$$

where P is the <sup>1</sup>DD peak amplitude at 292 nm, C is the concentration and r is the correlation coefficient.

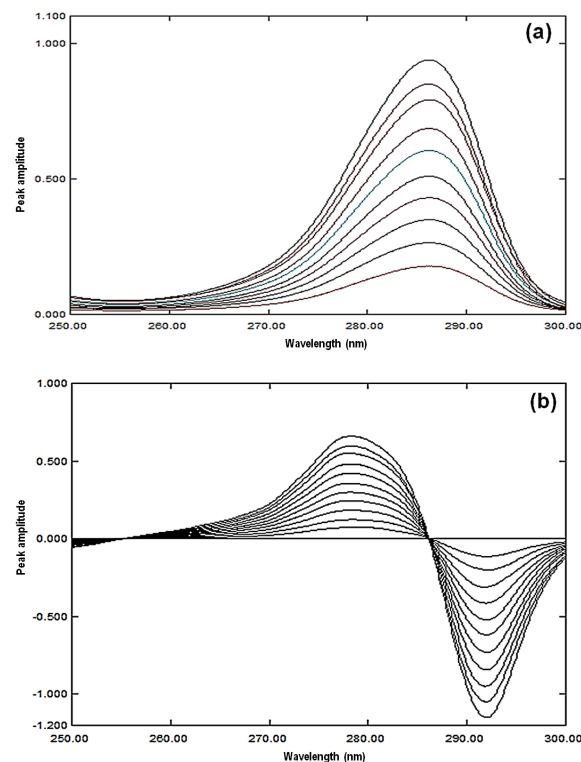


Figure 4. Ratio (a) and first derivative of ratio spectra <sup>1</sup>DD (b) of 6.00-22.00 µg/mL of oxymetazoline hydrochloride, using sodium cromoglycate (10.00 µg/mL) as a divisor.

#### 3.2.3. Method C: Ratio difference method (RD)

Several approaches have been developed to remove the overlapping constant in the ratio spectrum, either by using certain order derivative or through a sophisticated subtraction followed by a multiplication procedure. The latter was capable of determining only the component with the less extended spectrum in the mixture [37]. A simple innovative method namely ratio difference was developed capable of determining OXMT in binary mixture with SCG with minimal data processing and high selectivity, regardless which component has more extended spectrum [38-41]. The utility of ratio difference method is to calculate the unknown concentration of a component of interest present in a mixture containing both component of interest and an unwanted interfering component.

For the determination of the concentration of the component of interest by the ratio difference method, the only requirement is the contribution of the two components at the two selected wavelengths  $\lambda_1$  and  $\lambda_2$ , where the ratio spectrum of the interfering component shows the same amplitudes (constant) but the component of interest shows significant difference in these two amplitude values at those two selected wavelengths with concentration.

For the determination of OXMT, two wavelengths were selected (286.6 and 294.0 nm), where the ratio spectrum of SCG showed the same amplitudes (constant) but the ratio spectrum of OXMT showed significant difference in these two amplitude values at these two selected wavelengths with concentration (Figure 5). Correlation was obtained between  $\Delta P$  286.6-294.0 nm and the corresponding concentration of OXMT. The respective regression equation was found to be:

$$\Delta P \text{ 286.6-294 nm} = 0.0592 C - 0.0027 \quad r = 0.9999 \quad (4)$$

where,  $\Delta P$  286.6-294.0 nm is the difference in amplitude at 286.6 and 294.0 nm, C is the concentration in  $\mu\text{g/mL}$  and r is the correlation coefficient.

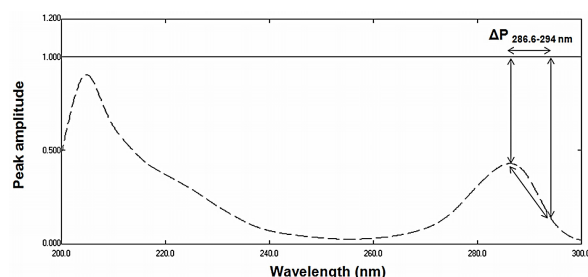


Figure 5. Ratio spectra of 10.00  $\mu\text{g/mL}$  of each of oxymetazoline hydrochloride (---) and sodium cromoglycate (—) using 10.00  $\mu\text{g/mL}$  sodium cromoglycate as a divisor.

### 3.2.4. Method D: Ratio subtraction method (RS)

El-Bardicy *et al.* [37] introduced the RS method which could be applied for determination of several drugs in their binary mixtures without prior separation. This method could be applied for determination of binary mixture of SCG (X) and OXMT (Y) where the spectrum of (X) is more extended than the other component (Y), as shown in Figure 2. The determination of (Y) was achieved by scanning the zero order absorption spectra of the laboratory prepared mixtures (X and Y) in methanol, then dividing them by a carefully chosen concentration (10.00  $\mu\text{g/mL}$ ) of standard (X) using X0 as a divisor to produce a new ratio spectra that represents  $Y/X_0 + X/X_0$  (constant), as shown in Figure 6. The constant value could be determined directly from the curve by the plateau straight line (300-350 nm) which was parallel to the wavelength axis in the region where (X) was extended; then subtraction of the absorbance values of these constants ( $X/X_0$ ) in plateau; (Figure 7), followed by multiplication of the obtained spectra by the divisor (X0). Finally, the original spectra of (Y) could be obtained, (Figure 8) and were used for direct determination of (Y) at 282.6 nm in the mixtures in the concentration range of 4.00-22.00  $\mu\text{g/mL}$ , while the concentration of (X) could be calculated without any interference, at its  $\lambda_{\text{max}}$  320.6 nm. A linear relationship was obtained between absorbance of OXMT at  $\lambda = 282.6$  nm and the corresponding concentration in the range of 4.00-22.00  $\mu\text{g/mL}$ . The linear regression was found to be:

$$A = 0.0385 C - 0.0015 \quad r = 0.9999 \quad (5)$$

where A is the absorbance at 282.6 nm, C is the concentration and r is the correlation coefficient.

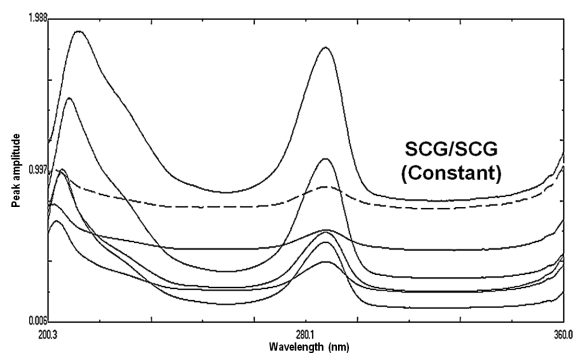


Figure 6. Ratio spectra of different lab mixtures of oxymetazoline hydrochloride and sodium cromoglycate using 10.00  $\mu\text{g/mL}$  sodium cromoglycate as a divisor.

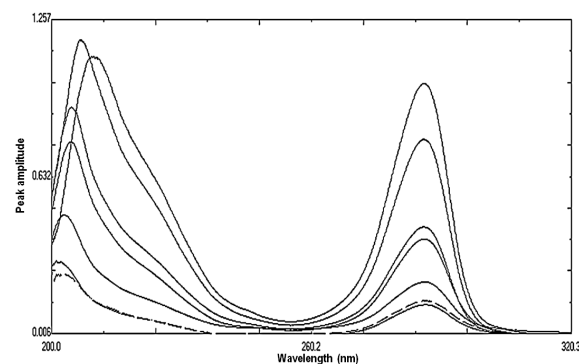


Figure 7. Ratio spectra of different lab mixtures of oxymetazoline hydrochloride and sodium cromoglycate using 10.00  $\mu\text{g/mL}$  sodium cromoglycate as a divisor after subtraction of the constant at plateau.

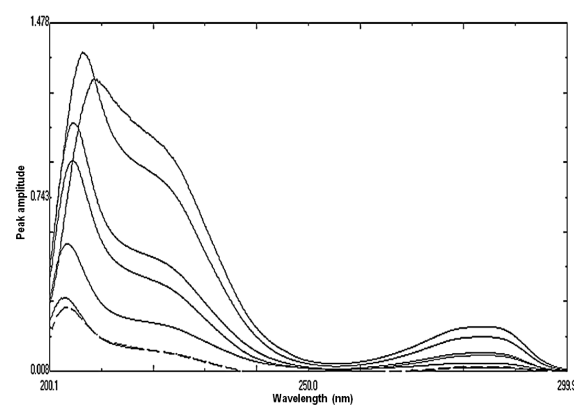


Figure 8. Ratio spectra of different lab mixtures of oxymetazoline hydrochloride and sodium cromoglycate using 10.00  $\mu\text{g/mL}$  SCG as a divisor after subtraction of the constant at plateau followed by multiplication of the obtained spectra by the divisor.

This method showed maximum accuracy and reproducibility over the other methods since it obtains the original spectra of the component in the binary mixture in its zero order and allows its determination at its  $\lambda_{\text{max}}$ . On the other hand, the disadvantage is that it requires the extension of one of the two components of the mixture. Thus, it is limited to determination of the non-extended component only.

**Table 1.** Assay parameters and method validation obtained by applying the proposed spectrophotometric methods for determination of sodium cromoglycate (SCG) and oxymetazoline hydrochloride (OXMT) in binary mixtures.

Method	SCG		OXMT		
	[ <sup>0</sup> D] method $\lambda = 320.6 \text{ nm}$	[ <sup>1</sup> D] method $\lambda = 289.2 \text{ nm}$	[ <sup>1</sup> DD] $\lambda = 292.0 \text{ nm}$	[RDSM] ( $\Delta P 286.6-294.0 \text{ nm}$ )	[RSM] $\lambda = 282.6 \text{ nm}$
Calibration range ( $\mu\text{g/mL}$ )	1.00-25.00	4.00-22.00	4.00-22.00	6.00-22.00	4.00-22.00
Slope	0.0454	0.0083	0.0592	0.0525	0.0068
Intercept	0.0056	0.0027	- 0.0027	- 0.0028	0.0007
r	1.0000	0.9995	0.9999	0.9999	0.9994
LOD ( $\mu\text{g/mL}$ )	0.24	0.53	0.41	0.77	0.46
LOQ ( $\mu\text{g/mL}$ )	0.68	1.60	1.24	2.31	1.39
Accuracy (Mean $\pm$ RSD) *	99.86 $\pm$ 1.602	101.01 $\pm$ 1.248	99.79 $\pm$ 0.985	100.36 $\pm$ 1.086	99.69 $\pm$ 1.487
Precision (RSD)	0.540	1.000	1.020	1.107	0.932
Repeatability intermediate precision	0.613	0.459	0.987	1.122	0.732

\*Average of three determinations.

**Table 2.** Determination of sodium cromoglycate (SCG) and oxymetazoline hydrochloride (OXMT) in laboratory prepared mixtures by the proposed spectrophotometric methods.

Concentration ( $\mu\text{g/mL}$ )		SCG		OXMT		
SCG	OXMT	[ <sup>0</sup> D] $\lambda = 320.6 \text{ nm}$	[ <sup>1</sup> D] $\lambda = 289.2 \text{ nm}$	[ <sup>1</sup> DD] $\lambda = 292.0 \text{ nm}$	[RDSM] ( $\Delta P 286.6-294.0 \text{ nm}$ )	[RSM] $\lambda = 282.6 \text{ nm}$
12.00	4.00	98.18	98.74	102.09	-	99.16
2.00	10.00	99.93	98.18	102.04	98.45	98.74
4.00	8.00	99.15	98.77	98.74	98.18	98.77
12.00	16.00	100.67	99.12	98.77	102.11	99.93
6.00	18.00	102.01	99.15	99.15	100.67	100.60
24.00	6.00	100.60	98.77	100.00	100.97	98.19
* Mean $\pm$ RSD		100.09 $\pm$ 1.331	98.79 $\pm$ 0.346	100.13 $\pm$ 1.567	100.08 $\pm$ 1.699	99.23 $\pm$ 0.877

\*Average of three determinations.

**Table 3.** Determination of sodium cromoglycate (SCG) and oxymetazoline hydrochloride (OXMT) in Nasocrom<sup>®</sup> nasal spray by the proposed spectrophotometric methods and the application of standard addition technique.

Method	SCG		OXMT		
	[ <sup>0</sup> D] $\lambda = 320.6 \text{ nm}$	[ <sup>1</sup> D] $\lambda = 289.2 \text{ nm}$	[ <sup>1</sup> DD] $\lambda = 292 \text{ nm}$	[RDSM] ( $\Delta P 286.6-294 \text{ nm}$ )	[RSM] $\lambda = 282.6 \text{ nm}$
Nasocrom nasal spray B.N. 11087 *	103.31 $\pm$ 1.991	99.08 $\pm$ 0.733	100.82 $\pm$ 1.775	102.08 $\pm$ 1.733	102.00 $\pm$ 0.000
Recovery% of standard added	99.97 $\pm$ 1.431	98.25 $\pm$ 1.313	99.75 $\pm$ 0.712	100.09 $\pm$ 1.136	99.77 $\pm$ 1.719

\* Claimed to contain 2 g SCG and 0.025 g OXMT per 100 mL.

Another drawback was observed upon analysis of mixtures containing low concentrations of the divisor, where the calculation of the constant value through plateau region was critical due to low signal to noise ratio.

### 3.3. Method validation

Validation was done according to ICH guidelines [42].

#### 3.3.1. Linearity

The linear regression data for the calibration curves showed good linear relationships. The correlation coefficients for the five proposed methods ranged from 0.9994 to 1.0000 as summarized in Table 1.

#### 3.3.2. Accuracy

The accuracy of the five methods was tested by analyzing freshly prepared solutions of the two drugs (7.50, 10.00 and 12.50  $\mu\text{g/mL}$ ) in triplicate. The percentage recoveries for each drug were calculated and summarized in Table 1.

#### 3.3.3. Range

The calibration range was established through considerations of the practical range necessary according to adherence to Beer's law and the concentration of SCG and OXMT present in the pharmaceutical preparation to give accurate precise and linear results (Table 1).

#### 3.3.4. Precision

Three concentrations of SCG and OXMT (7.50, 10.00 and 12.50  $\mu\text{g/mL}$ ) were analyzed in triplicate in the same day and in three successive days using the proposed methods in order

to determine the Repeatability and Intermediate precision, respectively. Relative standard deviation (RSD) values were calculated for each sample and summarized in Table 1.

#### 3.3.5. Specificity

The specificity of the methods was assessed by the analysis of different laboratory prepared mixtures of SCG and OXMT within the linearity range. Satisfactory results were obtained as shown in Table 2.

#### 3.4. Application to Nasocrom<sup>®</sup> nasal spray and standard addition

The five proposed methods were successfully applied for the determination of the studied drugs in their nasal spray dosage form. The results which are average of three determinations are shown in Table 3. The validity of the proposed methods was further assessed by applying the standard addition technique for the analysis of Nasocrom<sup>®</sup> nasal spray and results were summarized in Table 3.

#### 3.5. Statistical analysis

Results obtained from the proposed methods were statistically compared to those obtained by applying the USP methods [36] which are spectrophotometric method and HPLC for SCG and OXMT, respectively. Results showed no significant difference as observed from the calculated t and F values (Table 4). To compare the ability of the proposed methods for the determination of OXMT, the results obtained by applying the proposed methods were subjected to statistical analysis using one way ANOVA test, there was no significant difference ( $F < F_{\text{crit}}$ ) between all the proposed methods and the official one [36] as summarized in Table 5.

**Table 4.** Statistical analysis of the proposed methods and Official method for sodium cromoglycate (SCG) and oxymetazoline hydrochloride (OXMT) in their pure powder form.

Method	SCG		OXMT				Official method <sup>b</sup>
	Official method <sup>a</sup>	[ <sup>0</sup> D] $\lambda = 320.6 \text{ nm}$	[ <sup>1</sup> D] $\lambda = 289.2 \text{ nm}$	[ <sup>1</sup> DD] $\lambda = 292 \text{ nm}$	[RDSM] ( $\Delta P 286.6\text{-}294.0 \text{ nm}$ )	[RSM] $\lambda = 282.6 \text{ nm}$	
Mean	101.50	99.86	101.01	99.79	100.36	99.69	99.93
S.D	1.005	1.600	1.261	0.983	1.090	1.482	1.005
Variance	1.010	2.561	1.589	0.966	1.188	2.196	1.010
n	5	5	5	5	5	5	5
Student's t-test (2.306) <sup>c</sup>	-	1.939	1.499	0.222	0.645	0.306	-
F-value (6.388) <sup>c</sup>	-	2.535	1.573	0.957	1.176	2.175	-

<sup>a</sup> Direct absorbance measurement at  $\lambda_{\text{max}}$  326 nm using Sodium phosphate buffer (pH = 7.4) as a blank [36].

<sup>b</sup> HPLC method; mobile phase: water: methanol: 1 M sodium acetate: glacial acetic acid (46:40:10:4) with UV detection at 280 nm [36].

<sup>c</sup> Figures in parentheses are the corresponding tabulated values at  $p = 0.05$ .

**Table 5.** Results of ANOVA (one way) for comparison of the proposed methods and the official one for determination of oxymetazoline hydrochloride.

Source of variation	SS	df	MS	F	p-value	F crit.
Between groups	5.873	4.000	1.468	1.052	0.406	2.866
Within groups	27.911	20.000	1.396			
Total	33.784	24.000				

Official method: HPLC method; mobile phase: water: methanol: 1 M sodium acetate: glacial acetic acid (46:40:10:4) with UV detection at 280 nm [36].

#### 4. Conclusion

We can conclude that the proposed methods are accurate, sensitive, selective and precise. Furthermore they are simple and do not require any sophisticated techniques or instruments. Therefore they are effective methods that can be used for the routine analysis of SCG and OXMT in their pure forms and in their available dosage form without prior separation.

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