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Different spectrophotometric methods of operating ratio spectra for analyzing pharmaceutical combinations of loratadine and dexamethasone

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ABSTRACT

Two different ratio spectrophotometric methods are introduced for the concurrent dedication of a binary combination of Dexamethasone (DEX) and Loratadine (LOR) in laboratory prepared combinations and pharmaceutical dosage form directly. Both methods are simple and do not need advanced methods or instruments. They are also sensitive and selective and may be utilized for routine analysis of DEX and LOR in their available dosage form without earlier separation. The methods are suitable and valid also for application in research facilities that don't have liquid chromatographic instruments. Method (I) is ratio derivative spectrophotometry (RDM), Method (II) is ratio subtraction (RSM) coupled with extended ratio subtraction method (EXRSM). The mathematical clarification for both methods is explained. Calibration curves of the two methods are linear in the concentration ranges between 3.0-25.0 µg /ml and 7.5-40.0 µg /ml for DEX and LOR in 0.1N MethanolicHCl, respectively. Both methods are validated as stated by the International Council for Harmonisation (ICH) guidelines where accuracy, precision, and repeatability are found to be within acceptable limits.

Keywords: Dexamethasone, Loratadine, Extended ratio subtraction method, Ratio subtraction method, Ratio Spectra Derivative spectrophotometry, Ratio spectra.

1. INTRODUCTION

Loratadine (LOR) is ethyl 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-1-piperidinecarboxylate [1] (Fig.1a). Its chemical formula $C_{22}H_{23}ClN_2O_2$ with molecular weight of 382.9g/mol[2]. It is a second-generation [3] ,non-sedating, histamine-1-receptor antagonist with effect on seasonal and perennial allergic rhinitis, has shown effective manipulation of asthma symptoms, improved pulmonary function, and long duration action in patients with allergic bronchial asthma[4].

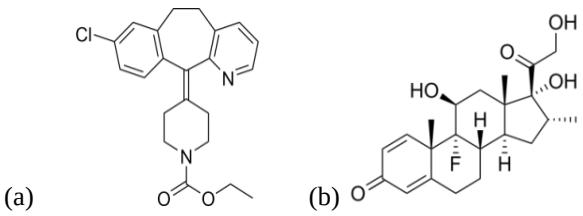

Fig 1: (a) Chemical structure of loratadine, (b) Chemical structure of dexamethasone

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Dexamethasone (DEX) has a chemical name of (8S,9R,10S,11S,13S,14S,16R,17R)-9-fluoro-11,17-dihydroxy-17-(2-hydroxyacetyl)-10,13,16-trimethyl-6,7,8,11,12,14,15,16-octahydrocyclopenta[a]phenanthren-3-one(Fig.1 b).Its chemical formula is $C_{22}H_{29}FO_5$ with a molecular weight of 392.5 g/mol [5]. It is a corticosteroid fluorinated at position 9 that relieves inflammation (swelling, heat, redness, and pain) [6],it is used to treat arthritis, blood/hormone/immune system disorders and certain cases of respiratory problems as in COVID- 19 [7] , also has direct effects on cell growth of solid tumors, like prostate and carcinomas[8]. It is conjointly used as a check for adrenal gland disorder (Cushing's syndrome) [9].

A combination of an antihistamine (loratadine) plus a systemic corticosteroid (dexamethasone) is to treat allergic conditions that, due to their severityor because they have not been controlled with loratadine alone, require associated treatment. It is used to relief of symptoms of acute and chronic allergic reactions: seasonal rhinitis, urticaria, allergic conjunctivitis, rhinopharyngitis, laryngotracheobronchitis, hay fever, drug or food allergy and contact eczema[10,11]

Literature survey showed that LOR was determined by many different methods which are high performance liquid chromatography[12-14], spectrophotometry[15-17] Successive and Progressive Spectrophotometric Resolution[18], RP-TLC/densitometric method [19],in-line potentiometric sensor[20], non-aqueous titrimetric assay [21],novel electrochemical sensoron silicon carbide nanoparticles modified glassy carbon electrode[22] and capillary zone electrophoresis [23]. While; DEX was determined by many different methods which are high performance liquid chromatography [24-26] Spectrophotometry[27,28], Fullerene-C60-modified edge plane pyrolytic graphite electrode[29], Highly sensitive voltammetric determination on amalgam film electrode[30]and Liquid Chromatography[31,32].

The literature revealed that there were no analytical methods reported for simultaneous dedication of both drugs combined together. The development and evaluation of spectrophotometric methods can reduce the time and cost of the analysis.

Several spectrophotometric methods followed by mathematical manipulations have been developed for resolving mixtures of compounds with overlapping spectra, e.g. simultaneous equation method[33], difference spectrophotometry[34,35], absorbance ratio spectra method[36,37], dual wavelength method[38,39], derivative spectrophotometry[40,41], Ratio Spectra Derivative spectrophotometry[42-44], double divisor ratio spectra derivative method[45], successive Ratio Spectra Derivative spectrophotometry[46], Q-absorbance ratio[47], isosbestic point method[34], absorpitivity factor method [48], ratio subtraction coupled with extended ratio subtraction method[49-51], and mean centering of the ratio spectra[52].

The aim of this manuscript is the analysis of the mixture of LOR and DEX using Ratio Spectra Derivative spectrophotometry (RDM) and ratio subtraction coupled with extended ratio subtraction method (EXRSM) as they are partially spectral overlapped.

This study reveals the importance of the newly developed spectrophotometric methods; Ratio Spectra Derivative Spectrophotometry, Ratio subtraction coupled with extended ratio subtraction method; for the spectral resolution of multicomponent combinations with overlapped spectra as they enable us for the concurrent dedication of both LOR and DEXaccurately and precisely in laboratory prepared combination and pharmaceutical dosage form and without prior separation.

2. EXPERIMENTAL

2.1. Apparatus and software

Spectral measurements were carried out on a Shimadzu (UV-1800), UV-VIS double beam spectrophotometer, fitted with 1.0 cm quartz cells and connected to a Hewlett-PackardW2072a computer equipped with UV-Probe 2.33 software which provides the ability of data manipulation for smoothing, dividing, deriving and subtracting.Absorption spectra were recorded over wavelength range 200-400 nm.

2.2. Materials and solvents

– **Pure drugs**

Reference standard of loratadine(LOR) was kindly given by Sigmatec Company for Pharmaceutical Industries (Quesna, Menofia, Egypt). Its purity was found to be 100.02%±1.017 (n=6) as assayed according to the USP official method [53].Reference standard of dexamethasone(DEX) was kindly given by Sigmatec Company for Pharmaceutical Industries (Quesna, Menofia, Egypt). Its purity was found to be 99.71% ± 0.84 (n=6) as assayed according to the USP official method[54].

– **Solvents**

Methanol : (Sigma Aldrich 99.8 % analytical grade), HCl : (37%, Merck, analytical grade).

– **Dosage forms**

Dexaprof D®labeled to contain 0.5mg dexamethasone and 5.0 mg loratadine per tablet[10].**Dexalor®** labeled to contain 2.0 mg dexamethasone and 10.0 mg loratadine per tablet[11].But as both drugs were not available in local market so a laboratory prepared combination resembling dosage form was prepared.

– **Excipients of tablet**

Magnesium stearate (ALEC Arabic lab. Equ.Co.), and microcrystalline cellulose (avicel) (Inter Trade Co.), corn starch (Universal laboratories), lactose (Iso-Chem Fine chemicals), starch glycolate sodium (Inter Trade Co.) were kindly given by Pharmaceutical Technology Department, Faculty of Pharmacy, Tanta University.

2.3. Stock and working standard solutions

Stock standard solutions

Accurately weighed 50.0 mg of LOR and 50.0 mg of DEX were independently transferred into 50.0 mL volumetric flasks and dissolved in 20.0 ml of methanol and then the volume was completed up to 50.0 mL by the same solvent to get a final concentration of 1.0 mg /ml for LOR and DEX.

Working standard solutions

An aliquot of 10.0 mL of either LOR or DEX stocksolutions was taken and diluted to 100.0 ml using 0.1 N HCl to obtain working solutions of a concentration 100.0 µg/ml each. In two separate series of 10.0 ml volumetric flasks; different volumes were accurately transferred from LOR and DEX standard working solution (100.0 µg/ml) then completed to volume with 0.1 N HCl to obtain solutions of concentration equivalent to 7.5 – 40.0 µg/ml for LOR and 3.0 –25.0 µg/ml for DEX.

3. General recommended procedures

3.1. Spectral characteristics of loratadine (LOR)and dexamethasone(DEX)

The zero-order absorption spectrum of 30.0 µg/ml LORand 3.0 µg/ml DEX in 0.1 N MethanolicHCl were scanned over the range of 200-400 nm against 0.1N MethanolicHCl as blank and the superimpose of the two spectra were recorded.

LOR showed a maximum absorbance peak at 278.0 nm while DEX showed a maximum absorbance peak at 242.4 nm. The overlain spectra (Fig.2) showed partial overlap between the two drugs.

3.2. Calibration curves construction

Solutions of concentration equivalent to 7.5 – 40.0 µg/ml for LOR and 3.0 –25.0 µg/ml for DEX were prepared (as shown in 2.3) and scanned over wavelength range 200-400 nm, against 0.1 N MethanolicHCl as a blank and stored in the computer.

3.2.1. Ratio Spectra Derivative Spectrophotometry (method-1)

For the dedication ofDEX in existence of LOR, the already obtained spectra of DEX were divided by the smoothed spectrum of 10.0µg/mlLOR(Fig. 3).The first derivative spectra with Δλ of 4.0 nm and scaling factor of 10 were recorded. The first derivative peak amplitude of (DEX/LOR) was determined at 227.8 nm (Fig.5).

For the dedication of LOR in existence of DEX, the already obtained spectra of LOR are divided by the spectrum of 4.0µg/mlDEX and smoothed by Δλ of 2.0 nm (Fig. 4), following the first derivative spectra with Δλ of 4.0 nm scaling factor of 1was recorded. The first derivative peak amplitude of (LOR/DEX) is determined at 291.1 nm (Fig. 6).

Two calibration curves were created representing the peak amplitudes at 227.8 and 291.1 nm against their corresponding concentrations (µgmL-1) of DEX and LOR; respectively and the regression equations were calculated.

3.2.2. Extended Ratio Subtraction Spectrophotometry (method- II)

Two calibration curves were created representing the absorbance of the zero order spectra of DEX and LOR at 242.4 and 278.0 nm; respectively against their corresponding concentrations then the regression equations were determined.

4. Application of method (I) and method (II)

4.1. Dedication of combination of LOR and DEX

A set of combinations containing both drugs at different ratios of LOR : DEX (40.0:4.0, 30.0:3.0, 20.0:10.0, 10.0:10.0 , 10.0:20.0 and 20.0:4.0 µg/ml) were set up by moving various aliquots from each of LOR and DEX working standard solutions (100.0 µg/ml) into 10.0 ml volumetric flask and so finishing the volume with 0.1 N MethanolicHCl. These combinations would be examined for accuracy and precision calculation of both methods.

A set of combinations containing both drugs; LOR at a fixed concentration (10.0 µg/ml) and DEX concentrations ranging from 3.0 µg/ml-25.0 µg/ml were set up by moving a constant aliquots from LOR and various aliquots from DEX working standard solutions (100.0 µg/ml) into 10.0 ml volumetric flask and so finishing the volume with 0.1 N MethanolicHCl. These combinations would be examined for confirming the reliability of method-II.

4.2. Dedication of LOR and DEX in laboratory prepared combination resembling marketed formulation

LOR is co-formulated with DEX as in Dexaprof D® tablets. The fixed dose combination of LOR and DEX is not available in the local market; synthetic combination equivalent to twenty tablets was prepared. It contains 100.0 mg LOR, 10 mg DEX, 60.0 mg magnesium stearate (as a lubricant), 60.0 mg starch glycolate sodium (as a disintegrant), 150.0 mg corn starch (as a disintegrant and binder), 620.0 mg lactose (as a filler or diluent) and 2000.0 mg avicel (as a direct compression filler).

The weight equivalent to one synthetic tablet (150 mg) was transferred to a 50.0 ml volumetric flask, first dissolved it in 30.0 ml 0.1 N MethanolicHCl, and sonicated for 15 minutes, allowed to settle down then completed to the required volume using the same solvent. It was filtered and the first 10 ml of the filtrate was removed. Then another dilution was prepared in the obtained linearity range using the same solvent. A 3.0 ml of the filtrate was transferred into a 10 ml volumetric flask and completed to 10ml with 0.1 N MethanolicHCl to obtain a solution containing; 30 µg/ml LOR and 3 µg/ml DEX. The solution was examined using the identified methods. The concentrations of both drugs would be determined from their corresponding regression equations.

5. RESULTS AND DISCUSSION

The aim of this study was to develop a simple, sensitive, rapid and precise spectrophotometric method for the concurrent dedication of a binary combination of LOR and DEX in their tablet dosage form and validated as defined by the ICH guidelines[55]. The key issue was the analysis of this laboratory prepared combination that has an overlapping spectrum with a significance gap between the absorptivities of the two drugs.

Unfortunately; this overlapping hinders their simultaneous dedication. The D0 spectra of LOR and DEX presented certain overlapping (Fig. 2) that permitted the dedication of LOR in existence of DEX at 306.0 nm, but hindered the dedication of DEX in existence of LOR.

5.1. Method(I)

The most benefit of the Ratio Spectra Derivative spectrophotometry method is the ability of using the highest value wavelength of either a maximum or a minimum signal. Also, the presence of several maxima and minima signals which allows the dedication of the drugs in the presence of others.

The main constraints that affect the shape of the Ratio Spectra Derivative spectra are the wavelength selection, the divisor concentration, the Δλ over which the derivative is attained and the smoothing function were carefully optimized.

5.1.1. Development of the method

Previous trials for various levels of concentrations of LOR and DEX divisors were tested before developing the method. An accurate select of both standard divisors and working wavelengths is essential for many important reasons as in the wavelength choice where the standard spectrum absorbance used as divisor almost being near zero, the ratio spectra noise is increased. Accordingly, a specific spectra overlap in the area of working wavelengths is preferred. So, any increase or decrease in the concentration of the divisor will cause that the resulting derivative values (hence, the calibration curves slope) are proportionately decreased or increased, respectively by a potential variation in each of linearity range and sensitivity.

To select the best conditions various trials were tested to get the best results in terms of average percent recovery of DEX and LOR concentrations, signal-to-noise ratio, repeatability and sensitivity were obtained. Using standard spectra of (3.0 and 4.0 µg/ml) DEX and (7.5 and 10.0 µg/ml) LOR as divisors showed minimal differences. Standard spectra of 4.0 µg/ml of DEX and 10.0 µg/ml of LOR were selected because they gave best results concerned to accuracy.

The wavelength choice was tested as well. Good linearity was observed by measuring at 291.1 and 313.5 nm for LOR dedication and at 227.8 and 265.9 nm for DEX dedication. However; the percent recovery at 291.1 and 227.8 nm were better for LOR and DEX; respectively, that may be attributed to their higher signal to noise ratio.

The influence of delta lambda (Δλ for plotting the first derivative of the ratio spectra was also tested to attain the best wavelength interval. Different Δλ values were tried (2, 4, 8 and 16). Δλ affects shape, intensity, and position of peaks of the analyzed target analyte. For Δλ = 4 nm was selected as optimum value as it gave maximum peak heights with minimum noise LOR (Figure 3 and 4).

The peak amplitudes of the Ratio Spectra Derivative were then recorded at 291.1 nm for LOR (Fig. 6) and at 227.8 nm for DEX (Fig. 5) under the range of linearity for method validation.

5.2. *Method (II)*

The Extended Ratio Subtraction method starts after applying the Ratio Subtraction method [29]. The Ratio Subtraction method relies on that, for a combination of LOR and DEX, it was found that there is an extension for the spectrum of LOR (Fig. 2), the finding of DEX in the combination would be done by scanning the zero order spectra of the laboratory-prepared combinations (DEX + LOR) through dividing them by a divisor standard concentration LOR* (10 µg/ml smoothed spectrum). This divisor concentration was chosen because it was found to give the best regression over the linearity range. After division with the divisor standard concentration LOR* (10 µg /ml smoothed spectrum) a new ratio spectra is obtained and can be represented by (DEX/ LOR* + LOR/ LOR*) (Fig. 7a, S1a). Subtract the constants' values (LOR/ LOR*) in the plateau

region (290-320 nm) (Fig. 7b, S1b). Then multiply the newly obtained spectra by the divisor LOR∗ (10 µg/ml smoothed spectrum) (Fig. 7c, S1c) which will give a new spectra that should correspond to the original spectra of DEX. These obtained spectra are used for direct dedication of DEX at 242.4 nm by calculating the concentration using the regression equation that was previously obtained from plotting the absorbance spectra of the 0D curves of DEX at 242.4 nm versus the corresponding concentrations.

Similarly, the detection of LOR could be carried out by the extended ratio subtraction method by dividing these obtained spectra of DEX by a precisely selected divisor standard concentration DEX∗ (4 µg/ml) producing ratio spectra that represent the constants (DEX / DEX∗) in the plateau (200-280 nm). The scanned zero order absorption spectrum of the laboratory-prepared combinations (DEX + LOR) were divided by divisor DEX∗ (4.0 µg/ml) to produce a new ratio spectra which would be represented as follows (LOR/ DEX∗ + (DEX / DEX∗)(Fig. S2a). Then these constants (DEX / DEX∗) would be subtracted (Fig. S2b), then multiply the newly obtained spectra by the divisor DEX∗ (4.0 µg/ml) (Fig. S2c). At last the original spectra of LOR (Fig. S2c) would be obtained and used for direct dedication of LOR at 278.0 nm, calculating of the concentration using the regression equation that was previously calculated after plotting the absorbance spectra of the zero order curves of LOR at 278.0 nm versus the corresponding concentrations.

The extended ratio subtraction method has a favor that the extended drug in the combination could be dedicated at its λmax which could not be done by the previously established ratio subtraction method which had dedicated unextended drug only. So, the both methods are decided to be complementary to each other as the both constituents in the combination would be dedicated.

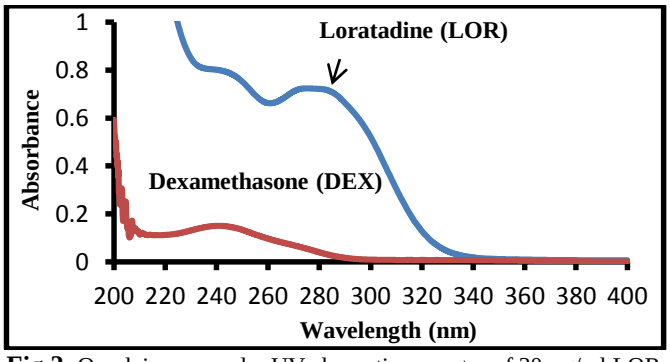

Fig.2. Overlain zero order UV absorption spectra of 30 µg/ml LOR (▬), 3µg/ml DEX (▬) with the same ratio as marketed formulation.

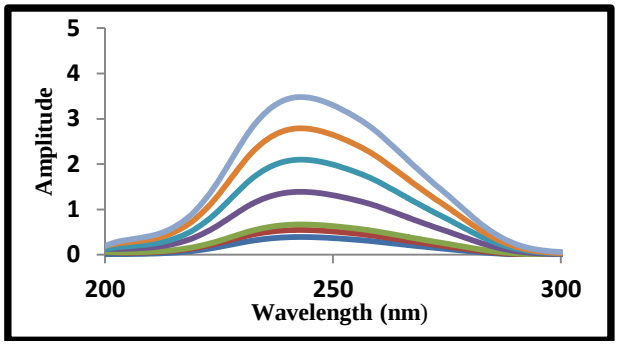

Fig. 3: Ratio spectra of DEX (3.0–25.0 µg/ml) using smoothed 10.0µg/ml of LOR as a divisor.

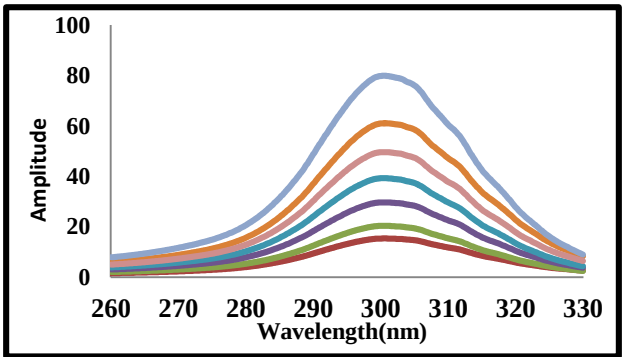

Fig. 4: Smoothed ratio spectra of LOR (7.5-40.0 µg /ml) using 4.0 µg/ml of DEX as a divisor.

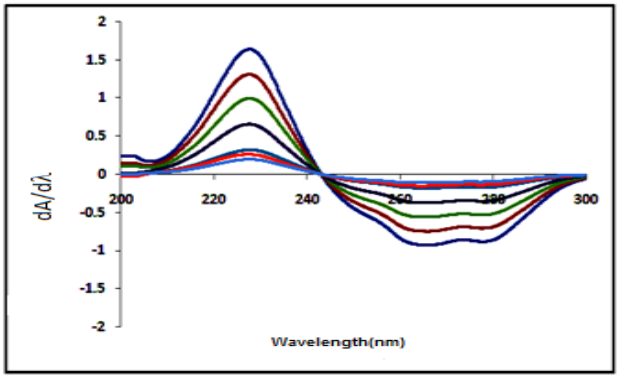

Fig. 5: First derivative ratio spectra of DEX (3.0 –25.0µg/ml) using smoothed 10.0 µg/ml of LOR as a divisor.

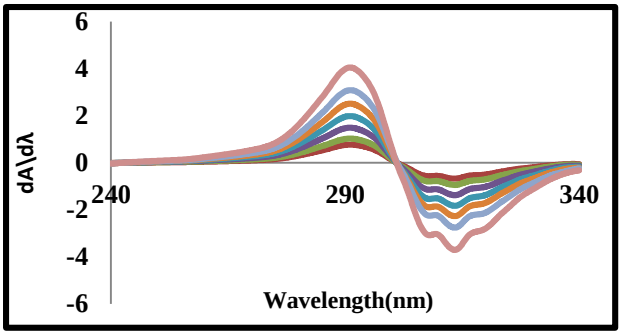

Fig. 6: First derivative of smoothed ratio spectra of LOR (7.5-40.0 µg /ml) using 4.0 µg/ml of DEX as a divisor.

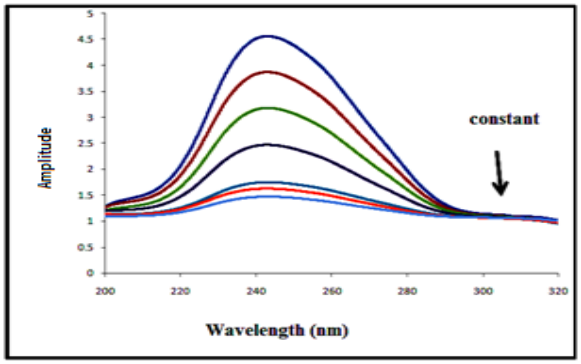

Fig. 7(a): Ratio Spectra of some laboratory prepared mixtures of DEX (3.0–25.0µg/ml) and LOR (10.0 µg /ml) using 10.0 µg /ml of LOR∗ as a divisor.

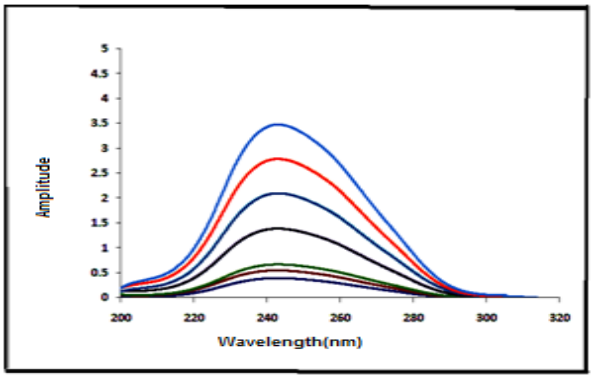

Fig. 7(b): Ratio Spectra of some laboratory prepared mixture of DEX (3.0–25.0µg/ml) and LOR (10.0 µg /ml) using smoothed 10.0 µg /ml of LOR∗ as a divisor after subtraction of the constant.

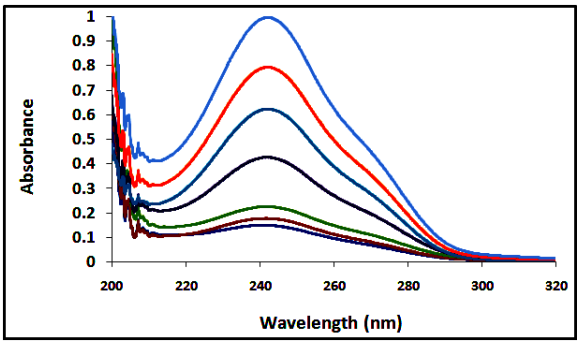

Fig. 7(c): The zero order absorption spectra of different concentrations of DEX obtained by the proposed ratio subtraction method for the analysis of laboratory prepared mixtures after multiplication by smoothed 10µg/ml of LOR∗ as a divisor.

6. METHOD VALIDATION

Validation of the suggested methods was assessed as stated by the ICH guidelines[55] as shown in tables 1-3.

6.1. Linearity and Range

The linearity of the methods was determined by analyzing seven concentrations of DEX and seven concentrations of LOR ranging from 3.0-25.0 µg/ml and 7.5-40.0 µg/ml, respectively. Each level of concentration was analyzed three times. The analysis was performed by the experimental conditions as discussed before. The linear regression equations are summarized in (Table 1).

6.2. Accuracy

Accuracy was studied by applying the proposed methods on three different levels of quality control samples from standard solutions of both drugs, the concentrations of samples were back calculated using the corresponding regression equations and then the percent recovery from the nominal concentration were calculated showing good accuracy. Results are summarized in (Table 2).

6.3. Precision

– **Repeatability (intra-day)**

Intra-day precision was studied by applying the proposed methods on three levels of quality control samples from standard solutions of both drugs with concentrations (10.0, 15.0 and 20.0 µg/ml), six replicate at each level of the three concentration levels were all analyzed in the same day. The relative standard deviations were calculated and shown in (Table 2).

– **Reproducibility (inter-day)**

Inter-day precision was carried out during the routine work of the research over three different days on the same three levels of concentrations chosen previously. Statistical evaluation of the relative standard deviations were calculated and shown in (Table 2).

6.4. Selectivity

Selectivity of the proposed methods for dedication of both drugs was examined by analyzing a set of laboratory binary mixtures with different ratios of LOR and DEX within the linearity range, including the ratio present in both pharmaceutical dosage forms mentioned previously. Reliable results were obtained and summarized in (Table 3)

Table 1: Linearity and regression equations of the proposed spectrophotometric methods

Drug	Method	Regression equation	Correlation coefficient(r)	Wavelength (nm)
Dexamethasone	**RDM**	y = 0.0655x - 0.0047	0.9998	227.8nm
	RSM	y = 0.0383x + 0.0369	0.9997	242.4nm
Loratadine	**RDM**	y = 13.977x + 1.9337	0.9998	291.1nm
	EXRSM	y = 0.0233x - 0.0094	0.9997	278.0nm

Where **RDM** is Ratio Spectra Derivative spectrophotometric method, **RSM** is ratio substraction spectrophotometric method and **EXRSM** is extended ratio substraction spectrophotometric method.

Table 2: Analytical parameters and method validation for determination of Dexamethasone and Loratadine by the proposed spectrophotometric methods

Parameter	Dexamethasone		Loratadine	
	RDM	**RSM**	**RDM**	**EXRSM**
Range (µg /ml)	3.0- 25.0	3.0- 25.0	7.5- 40.0	7.5- 40.0
Accuracy	99.91 ± 0.60	100.36 ± 0.838	99.84 ± 0.912	99.79 ± 0.899
Repeatability[a]	99.96 ± 0.45	100.70 ± 0.886	100.15 ± 1.30	100.65 ± 1.01
RSD%[a]	0.451%	0.880%	1.303%	1.009%
Reproducibility[b]	100.18 ± 0.791	100.29 ± 0.605	99.95 ± 0.516	100.55 ± 0.723
RSD%[b]	0.790%	0.604%	0.516%	0.719%

a: Intra-day (n=6), average of six replicate of three concentrations (10,15,20 µg/ml) analyzed within the same day.
b: Inter-day (n=6), average of three concentrations (10,15,20 µg/ml) repeated six times in six consecutive days.

Table 3: Determination of Dexamethasone and Loratadine in their binary laboratory mixtures by the proposed methods

Ratios		Dexamethasone (%Recovery ± SD)		Loratadine (%Recovery ± SD)	
DEX : LOR	**Conc. (µg /ml)**	**RDM**	**RSM**	**RDM**	**EXRSM**
1:10*	3:30*	100.78 ± 0.05	100.46 ± 0.03	99.91 ± 0.21	100.40 ± 0.42
1:10*	4:40*	100.01 ± 0.03	100.22 ± 0.05	99.82 ± 0.30	100.06 ± 0.36
1:5[#]	4:20[#]	101.15 ± 0.18	100.47 ± 0.46	98.97 ± 1.02	99.21 ± 0.87
1:1	10:10	99.69 ± 0.08	100.05 ± 0.09	99.41 ± 0.11	100.88 ± 0.11
2:1	20:10	100.59 ± 0.29	100.86 ± 0.19	100.20 ± 0.12	100.07 ± 0.12
1:2	10:20	99.51 ± 0.08	100.37 ± 0.12	99.71 ± 0.17	99.32 ± 0.14

*: The Ratio in Dexaprof D tablets,[#]: The Ratio in Dexalor tablets.
All calculations were done for nine determinations.

7. Application of proposed methods in assay of laboratory prepared combination resembling dosage form

The combined dosage form of DEX and LOR is available worldwide under the brand names of (Dexaprof D®, Dexalor®) however both drugs unfortunately are not available in Egypt, so a laboratory prepared combination containing the two drugs with all excipients that present in a tablet; resembling dosage form, was prepared as shown above.

The validity of the methods was examined by performing standard addition technique, which is carried out by adding various concentrations of the standard solutions of both drugs on the laboratory prepared dosage form then applying the proposed methods, it revealed that the methods were accurate and specific for dedication of both drugs in presence of their dosage form excipients as shown in (Table 4).

Effect of excipients

Excipients show no interference with the drugs absorption under wavelength 200-400 nm .The zero order spectrum of the mixture 3:30 and 4:40 (DEX: LOR) was overlaid on the zero order spectrum of the synthetic laboratory mixture (3:30) and (4:40) containing excipients and they were superimposed showing no differences(Fig.S3).

Statistical Analysis

Results achieved by the proposed methods for the dedication of LOR and DEX are statistically compared to those achieved by the official methods. The calculated t and F values were found to be less than their corresponding theoretical ones ensuring good accuracy and good precision (Table 5).

Table 4: Determination of Dexamethasone and Loratadine in their synthetic dosage form prepared in laboratory by the proposed methods and application of standard addition technique

Synthetic dosage form same ratio of Dexaprof D®	Claimed conc (µg/ml)	Standard addition			Recovery (mean ± s.d%)	
		Added conc (µg/ml)	Found conc (µg/ml)	Recovery %	Proposed method	Standard addition
RDM						
DEX	3	8	8.07	100.88		
		10	9.92	99.20		
		12	11.98	99.83	101.96 ± 0.02	99.97 ± 0.84
LOR	30	7.5	7.7	102.67		
		9	9.09	101.00	100.26 ± 0.18	101.65 ±0.88
		10	10.13	101.30		
RSM & EXRSM						
DEX	3	8	7.97	99.63		
		10	10.05	100.50	100.17 ± 0.02	100.40 ± 0.73
		12	12.13	101.08		
LOR	30	7.5	7.64	101.86		
		9	8.87	98.56	100.48 ± 0.15	99.94 ± 1.72
		10	9.94	99.40		

8. CONCLUSION

We would be able to conclude that the suggested methods are simple and do not need advanced methods or instruments. They are also sensitive and selective and may be utilized for routine analysis of DEX and LOR in their available dosage form without earlier separation. The methods are suitable and valid also for application in research facilities that don't have liquid chromatographic instruments.

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