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RESEARCH ARTICLE

Simultaneous Estimation of Chlorpheniramine Maleate and Glyceryl Guaiacolate in Pure and Capsule Dosage form by using different Spectrophotometric Methods

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ABSTRACT:
Chlorpheniramine Maleate (CPM) and Glyceryl Guaiacolate (GUA) are the β-lactum antibiotic drug. Sensitive, precise, accurate and simple, UV spectrophotometric methods have been developed for the simultaneous estimation of Chlorpheniramine Maleate (CPM) and Glyceryl Guaiacolate (GUA) in dosage form. Two spectrophotometric methods (simultaneoue equations and Q-Absorbance ratio) were applied for the determination of the drugs as mixture. The maximum absorbance of drug in solvent mixture composed of water – acetontrile – methanol in a ratio of (80% H_2O – 10% ACN – 10% MOH) was found to be at (261.4 nm and 273 nm) for CPM, GUA respectively, and the Q – isosbestic point was found at 270.4 nm. These wavelengths were selected for the analysis of drugs as mixtures standard and in the manufactured samples using the two developed methods. The methods were linear in the range of (1- 100) µg/mL for (CPM, GUA), with an R^2 of (0.9996) for CPM and GUA respectively in the mixture. Recovery means were found to be (99.79 % - 100.30 %) for the standard drugs CPM and GUA respectively and in formulating drugs was found to be (99.71 – 100.41 %). LOD and LOQ were established and found to be (0.1 and 0.33) for CPM and GUA respectively. The method was applied for the estimation of the active gradient of the drugs in different samples of manufactured dosage. The accuracy of method was validated by mean percentage recovery, which was found to be in the acceptable range.

KEYWORDS: Determination, Spectrophotometric, Simultaneous equation, Q-Absorbance ratio.

INTRODUCTION:
Cough can be caused by air pollution, smoking, allergic and etc. Cough medicines are used for relieve of cough. They are made up of one or more pharmaceutical active drugs. Cough preparations consist of antihistamines, antitussives, decongestants, expectorants and sleep aids[1]. In the recent years, combination dosage forms of Chlorpheniramine maleate (CPM) and Glyceryl Guaiacolate (GUA) as an agent to cure of cough is introduced. There is no analgesic agent to treat all forms of pain and there is no ideal analgesic factor, but each worker has advantages and disadvantages to distinguish him from the rest of the painkillers[2].

Chlorpheniramine maleate (CPM) IUPAC name [(RS)-3-(4-chlorophenyl)-3-(2- pyridyl) propyl methyl amine hydrogen maleate is a histamine H1 antagonist used in allergic reactions, hay fever, rhinitis, urticaria, and asthma. It is also effective against nausea and motion sickness, with its primary mechanism of action being its ability to reduce acetylcholine levels in the brain[3]. Glyceryl Guaiacolate (GUA) IUPAC name (RS)-3-(2-methoxyphenoxy) propane-1, 2-diol is an It is is an expectorant drug sold over the counter and usually taken orally to assist the bringing up (expectoration) of phlegm from the airways in acute respiratory tract infections. It is the component of numerous cough cold preparations available worldwide. It is soluble in water, dimethyl formamide and slightly soluble in ethanol. Guaifenesin has not been approved by the FDA for the treatment of fibromyalgia. Based on a small, non-blinded study, Glyceryl Guaiacolate has been promoted to facilitate conception, by thinning and increasing cervical mucus, during the few days before ovulation.[4] Many analytical methods were reported for the determination of these drugs in pharmaceuticals such as HPLC[5-8], GC[9], UV/Vis

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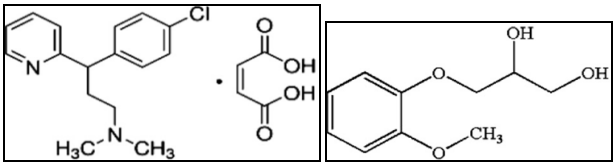
spectrophotometry[10-14], LC/MS[15] and LC-MS/MS[16-19]. The aim of this work was to develop the ease and accurate spectrophotometric method for the determination of the drug content in tablet samples from different pharmaceutical companies available in Iraqi pharmaceutical market, to give information about these products, which may or may not comply with the requirements of the standard method or other official methods, as shown in Fig. 1- a, b.



A B

Fig:1: A: Chlorpheniramine maleate (CPM) B: Glyceryl Guaiacolate (GUA)

MATERIALS AND METHODS:

Materials:

CPM and GUA were provided from Samara Drug Industries (SDI), Iraq. Different tablets samples were used as marketed formulation as in Table 3. Methanol HPLC grade (BDH) and freshly prepared deionized water was used throughout the experiment.

Apparatus:

UV - VIS spectrophotometer (UV-1700 Shimadzu – Japan), (Ultrasonic - China), sartorius balance (Germany), shaking water bath (Taiwan) and furnace (Germany) were used through this study.

Selection of common solvent:

Main criteria for media selection was solubility and stability, i.e. Chlorpheniramine maleate (CPM) and Glyceryl Guaiacolate (GUA) should be soluble as well as stable for sufficient time in selected media. The media used in reported method was water – acetonitrile – methanol in a ratio of (80 – 10 – 10) respectively, which was selected as analytical media for present work.

Preparation of drug stock solutions (1000 mg/L):

A 0.1g from each standard drug was weighed and dissolved in (80% H_2O – 10% ACN – 10% MOH), transferred to a 100mL volumetric flask separately, it was then sonicated for 10 minutes and the final volume of both the solutions were made up to 100mL with the solvent to get stock solutions containing 1000µg/mL each of CPM and GUA in two different 100mL volumetric flasks. More diluted solutions were prepared by simple dilution of stock solution of drugs.

Diluent:

By using the stock solution of 100µg/mL, subsequent dilution was carried out by withdrawing different aliquots (0.1 – 10) mL from standard solution were transferred into a series of 10mL calibrated volumetric flasks and all were made up to the mark with mobile phase in order to prepare working standard solutions of different concentrations (1 – 100) µg/mL.

RESULTS AND DISCUSSION:

Determination wavelength of maximum absorbance:

By appropriate dilution of two standard drug solutions with (80% H_2O – 10% ACN – 10% MOH), solutions containing 100µg/mL of CPM and 100µg/mL of GUA were scanned separately in the range of (200- 400) nm to determine the wavelength of maximum absorption for both the drugs. CPM and GUA showed absorbance maximum at 261.4nm (λ_1) and 273nm (λ_2) respectively, as shown in Fig. 2.

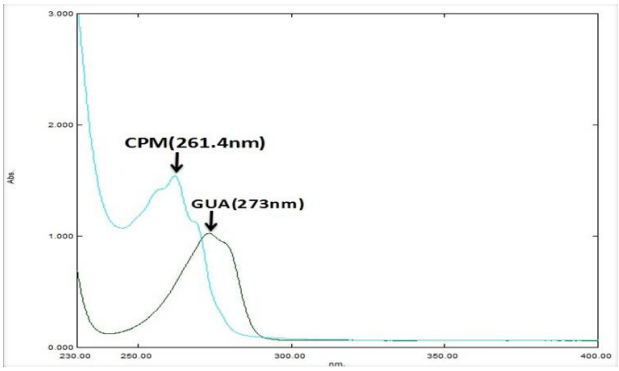


Fig: 2: UV-VIS Spectra of CPM and GUA

Method A: Simultaneous Equation Method:

Two wavelengths selected for the method are 261.4nm and 273nm that are absorption maxima of CPM and GUA in (80% H_2O – 10% ACN – 10% MOH), respectively. The stock solutions of both the drugs were further diluted separately with (80% H_2O – 10% ACN – 10% MOH), to get a series of standard solutions of 1-100µg/mL concentrations of CPM and 1- 100µg/mL concentrations of GUA. The absorbances were measured at the selected wavelengths for both the drugs at both wavelengths were determined as mean of Seventeen independent determinations. Concentrations in the sample were obtained by using following equations.

$$Cx = \frac{A1\ ay - A2\ ay1}{ax1ay2 - ax2ay1} \quad \text{Eq (i)}$$

$$Cy = \frac{A1\ ax - a2\ ax1}{ay1ax2 - ay2ax1} \quad \text{Eq(ii)}$$

Where, A1 and A2 are absorbance's of mixture at 261.4 nm and 273 nm respectively ax1 and ax2 are absorptivities of CPM at λ_1 and λ_2 respectively and ay1 and ay2 are absorptivities of GUA at λ_1 and λ_2 respectively. Cx and Cy are concentrations of CPM and GUA respectively.

Method B: Absorption Ratio Method (Q Method):
The solutions of CPM and GUA (10 µg /ml) were scanned in the range of 200 to 400 nm against (80% H_2O – 10% ACN – 10% MOH) as blank. For Q method, 270.4nm (isosbestic point) and 273nm (λ_{max} of Glyceryl Guaiacolate) were selected as wavelengths of measurements Fig. 3. Concentrations of CPM and GUA were determined using following equations[20].

Cx = (Qm - Qy). A1 / (Qx - Qy). ax1
and
Cy = (Qm - Qx). A1 / (Qy - Qx). ay1

Where
Qm = A2/ A1, Qx = ax2/ ax1, Qy = ay2/ ay1

Where, A1 and A2 are absorbance's of mixture at 270.4 nm and 273 nm respectively ax1 and ax2 are absorptivities of CPM at λ_1 and λ_2 respectively and ay1 and ay2 are absorptivities of GUA at λ_1 and λ_2 respectively. Cx and Cy are concentrations of CPM and GUA respectively.

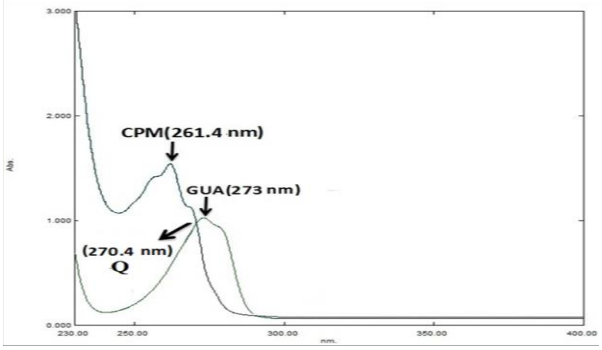


Fig: 3: Absorbance spectra for the drugs and Q - isosbestic point

Analytical method validation:
Additional parameters to be evaluated when demonstrating accuracy and precision are part of the method development and optimization process, or are performed during the validation process when demonstrating acceptable method performance. These parameters include limits of detection and quantification, linearity of the method, range, recovery, robustness and selectivity[21].

Linearity:
The linearity of measurement was evaluated by analysing different concentration of the standard solution of CPM and GUA. Absorbance of all solutions was measured at λ_{max} of each drug. For simultaneous equation method the Beer- Lambert's concentration range was found to be for 1-100µg/mL for CPM and 1-100µg/mL GUA, as shown in Fig. 4. The calibration graph were obtained by plotting absorbance versus known concentrations, and R^2 (0.9996) for the both drugs, indicating that there is a strong correlation between the variation of concentration and response. Linearity was determined by the regression analysis as shown in Table 1.

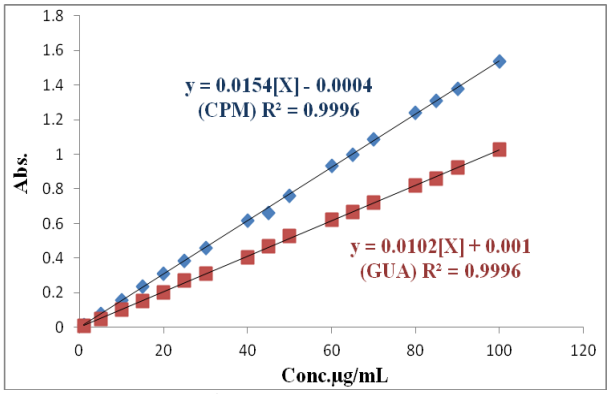


Fig: 4: Linearity curve for CPM and GUA

Table 1: Statistical calculations.

Statistical factors	Value	
	Chlorpheniramine Maleate	Glyceryl Guaiacolate
Linear equation	y= 0.0154 [X] + 0.0004	y = 0.0102[X] - 0.001
Slope (m)	0.0154	0.0102
Intercept	0.0004	0.001
Determination Coefficient R^2	0.9996	0.9996
Percentage linearity (R^2%)	99.96	99.96
Correlation Coefficient (r)	0.9998	0.9998
RSD	0.16	0.15
Linearity range µg/mL	1-100	1-100
Calculated (t) values $t_{cal.} = \frac{/r/\sqrt{n-2}}{\sqrt{1-r^2}}$	193.461>> 2.110	193.461 >> 2.110

Limit of Detection (LOD) and Limit of Quantization (LOQ):
The LOD and LOQ of a Chlorpheniramine maleate (CPM) and Glyceryl Guaiacolate (GUA) by proposed methods were determined using calibration standards. LOD and LOQ were calculated by gradual dilution of lowest concentration and as 3.0 LOD respectively. The results obtained are shown in Table 3.

ACCURACY:
CPM and GUA were determined at three different selected concentrations (6, 28, 55) µg/mL. The obtained results were tabulated in Table 2, which indicated that the proposed method for the determination of three drugs is quite satisfactory in reality with respect to the procedure and parameters calculated. The Optical characteristics data and validation parameters were tabulated in Table 2.

Table 2: Recovery study of CPM and GUA for the two methods.

Method	**Simultaneous estimation method**					
Drug	**Taken**	**Found**	**% Recovery ± SD**		**%Error**	**R.S.D n =3**
CPM	6	5.96	99.33	Mean = 99.79 S.D. =0.40	-0.67	0.18
	28	28.02	100.07		0.07	0.21
	55	54.98	99.96		-0.04	0.11
GUA	6	5.99	99.83	Mean = 99.91 S.D. = 0.12	-0.17	0.17
	28	27.96	99.86		-0.14	0.22
	55	55.03	100.05		0.05	0.15
Method	**Cut cross point method (Q– isosbestic)**					
Drug	Taken	Found	% Recovery ± SD		%Error	R.S.D n =3
CPM	6	6.06	101	Mean = 100.30 S.D. = 0.61	1	0.15
	28	28.01	100.04		0.04	0.19
	55	54.93	99.87		-0.13	0.10
GUA	6	6.01	100.17	Mean = 100.08 S.D. = 0.13	0.17	0.13
	28	27.98	99.93		-0.07	0.21
	55	55.07	100.13		0.13	0.10

Table 3: Optical characteristics data and validation parameters

Parameters	**Values for CPM**			**Values for GUA**		
Absorption maxima (λ max)	261.4 nm			273 nm		
Beer's law limit (µg/ml)	1-100			1-100		
Regression equation	y= 0.0154 [X] + 0.0004			y = 0.0102[X] - 0.001		
Correlation coefficient (R2)	0.9996			0.9996		
Molar absorptivity	λ1	λ2	λQ	λ1	λ2	λQ
	4264	1675	2672	1080	2034	1907
A(1%,1cm)	153.5			102.6		
Accuracy (%Recovery ± SD)	**Method A**	**Method B**		**Method A**	**Method B**	
	99.79 ± 0.40,	100.30 ± 0.61		99.91±0.12	100.08 ± 0.13	
LOD (µg/ml)	0.1			0.1		
LOQ (µg/ml)	0.33			0.33		
Precision	**Method A**	**Method B**		**Method A**	**Method B**	
Intraday*(Analyst 1)	100.05 ± 0.24,	99.96 ± 0.31		99.78 ± 0.15,	100.01± 0.34	
Interday*(Analyst 2)	100.43 ± 0.33,	99.69 ± 0.25		100.22± 0.38,	99.98 ± 0.16	

Quantitative assessment of drugs in tablets:

Different types of pharmaceutical formulations of drugs have been analyzed as described under recommended procedure, a good accuracy and precision were obtained as shown in Table 4. The absorbances of mixture solutions have concentration (5 and 0.1) µg/mL for GUA and CPM respectively, were measured at (261.4 and 273) nm for the simultaneous methods and at (270.4 and 273) nm for Q - method. The concentration of CPM and GUA present in the sample solution was calculated by using the equation generated for the two methods. Values were substituted in the respective formula to obtain concentrations. Obtained results were confirmed the reality, applicability and validity of the proposed method for the determination of CPM and GUA in pharmaceutical formulations. The results indicate that the recovery percentages for applying methods are with an acceptable range of (99.79 – 100.43%) for the quantity of drugs in tablets was accepted within the normal percentage according to official method.

Table 4: Estimated quantity of drugs in different formulated samples

Method	**Simultaneous estimation**				
Drugs name	**Drug Type**	**Amount taken mg/ 5 ml.**	**Mean amount found mg/ 5 ml.**	**%Mean amount Found**	**R.S.D n=3**
SOOLAN	CPM	1	0.997	99.71	0.13
	GUA	50	50.065	100.13	0.08
DECOPECT	CPM	1	0.999	99.94	0.15
	GUA	50	49.995	99.99	0.21
TUSSILET	CPM	1	1.001	100.07	0.10
	GUA	50	49.915	99.83	0.11
Method	**Cut cross point method (Q– isosbestic)**				
Drugs name	**Drug Type**	**Amount taken mg/ 5 ml.**	**Mean amount found mg/ 5 ml.**	**%Mean amount Found**	**R.S.D n=3**
SOOLAN	CPM	1	1.004	100.41	0.20
	GUA	50	50.08	100.16	0.13
DECOPECT	CPM	1	0.999	99.92	0.13
	GUA	50	49.975	99.95	0.16
TUSSILET	CPM	1	1.002	100.17	0.12
	GUA	50	49.935	99.87	0.10

CONCLUSION:

The most striking feature of this novel method is its simplicity, rapidity and economy, UV spectrophotometric method for the quantitative determination of CPM and GUA in standard and pharmaceutical formulated mixture samples simultaneously without any separation method. The new method can be employed for routine analysis in quality control drugs analysis. The described methods give accurate and precise results for the determination of CPM and GUA with recovery percentages range (99.00 – 100.43) for the drugs.

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AUTHORS' CONTRIBUTION:

All the authors have contributed equally

CONFLICT OF INTERESTS:

Declared none.

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