

DEVELOPMENT AND VALIDATION OF DOUBLE DIVISOR RATIO SPECTRA DERIVATIVE SPECTROPHOTOMETRY METHOD FOR TERNARY MIXTURE OF GUAIFENESIN, DEXTROMETHORPHAN HBR, AND DIPHENHYDRAMINE HCL IN TABLET DOSAGE FORM

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ABSTRACT

Objective: This study aimed to develop spectrophotometry method by double divisor ratio spectra derivative to determine the levels of guaifenesin (GUA), dextromethorphan hydrobromide (DMP), and diphenhydramine hydrochloride (DPH) in tablet dosage form using ethanol as solvent.

Methods: The method is based on the use of the coincident spectra of the derivative of the ratio spectra obtained using a double divisor (sum of two spectra) and measuring at either the maximum or minimum wavelengths. Then, the method was applied to determine the levels of GUA, DMP, and DPH in tablet dosage form.

Results: The application of double divisor ratio spectra derivative spectrophotometry method for the determination of GUA, DMP, and DPH was performed on the first derivative at $\Delta\lambda$ 2 (λ 280.0 nm, λ 286.1 nm, and 260.2 nm, respectively). The selection of wavelengths based on wavelengths gives the best result. The mean % recoveries were found to be in 100.60%, 99.95%, and 101.74% for GUA, DMP, and DPH, respectively.

Conclusion: The method is successfully applied to analyze GUA, DMP, and DPH in pharmaceutical formulation with no interference from excipients as indicated by the recovery study. All validation parameters were within the acceptable range.

Keywords: Guaifenesin, Dextromethorphan HBR, Diphenhydramine HCL, Double divisor ratio spectra derivative spectrophotometry.

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INTRODUCTION

Guaifenesin (GUA) is chemically known as (+)-3-(2-methoxy phenoxy)-propane-1,2-diol. Its empirical formula is $C_{10}H_{14}O_4$, which corresponds to molecular weight of 198.21. It has slight bitter aromatic taste. It is used to relieve the chest congestion. It controls the symptom but does not treat the cause of the symptom. It is an expectorant and thinning the mucus and clear the airways [1]. Dextromethorphan hydrobromide (DMP) is chemically known as ([+]-3-methoxy-17-methyl-9 α ,13 α ,14 α -morphinan), used in the form of the base or as the monohydrated hydrobromide salt. DMP is a cough suppressant which is found in many over-the-counter cough and cold remedies [2]. Diphenhydramine hydrochloride (DPH) is an antihistamine medication having the compound name 2-(diphenylmethoxy)-N,N-dimethylethylamine hydrochloride and has formula $C_{17}H_{21}NO.HCl$. DPH is used to treat sneezing, runny nose, watery eyes, hives, skin rash, itching, and other cold or allergy symptoms [3].

GUA was determined individually and with other compounds by spectrophotometry [1,4-6], reversed-phase high-performance liquid chromatography (RP-HPLC) [7,8] and HPLC [9-11] methods. DMP was determined individually and with other compounds by spectrophotometry [12-14], potentiometric [12], RP-HPLC [7], and HPLC [11] methods. DPH was determined individually and with other compounds by conductometry [15], spectrophotometry [16], and HPLC [11].

Double divisor ratio spectra derivative spectrophotometry method for simultaneous estimation is a simple, accurate, and cost-effectiveness [17]. According to the best of our knowledge, there is no published double divisor ratio spectra derivative spectrophotometry method for simultaneous estimation GUA, DMP, and DPH in their combination.

METHODS

Reagents and chemicals

All material and reagents were analytical grade. The raw standard of GUA was purchased from Zhejiang Halzhou Pharmaceutical, Linhai City, China, DMP and DPH were purchased from Beijing Taiyang Pharmaceutical Industry. Commercially available tablets were obtained from a local pharmacy.

Instruments and apparatus

The spectrophotometric measurements were carried out on a Shimadzu - ultraviolet (UV) 1800 spectrophotometer, matched quartz cells 1 cm and UV probe 2.42 software was used for all spectral measurements. Boeco analytical balance and Branson 1510 ultrasonicator was also used.

Preparation of standard solution

Accurately weighed 50 mg of GUA, DMP, and DPH standard was separately transferred into 100 mL volumetric flask and dissolved in ethanol to give solutions containing 500 μ g/mL GUA, DMP, and DPH.

Selection of analytical wavelength

The solutions of GUA, DMP, and DPH were prepared in diluent by appropriate dilution and spectrum was recorded. The absorption spectra of the solutions prepared at different concentrations of GUA (6–36 μ g/mL), DMP (9–25 μ g/mL), and DPH (9–25 μ g/mL) were scanned in the range of 200–400 nm. The double divisor value in various concentrations is calculated to selected wavelength range analysis.

Assay of tablet formulation by double divisor ratio spectra derivative spectrophotometry method

Content of 20 tablets was weighed accurately. A powder quantity equivalent to 75 mg GUA, 5 mg DMP, and 7.5 mg DPH was accurately weighed and transferred into volumetric flask of 100 mL capacity. 30 mL

of ethanol was transferred into this volumetric flask and sonicated for 10 min. The flask was shaken and volume was made up to the mark with diluent. The above solution was filtered through Whatman filter paper (0.45 μ). The solution was made up to the mark with diluent to give a solution containing 18 $\mu\text{g}/\text{mL}$ of GUA, 12 $\mu\text{g}/\text{mL}$ of DMP, and 18 $\mu\text{g}/\text{mL}$ of DPH. The resulting solution was analyzed by proposed method. The quantitation was carried out by keeping these values to the straight line equation of calibration curve.

Method validation

The method was validated based on linearity, accuracy, precision, limit of detection (LOD), and limit of quantification (LOQ). It was validated according to the International Conference on Harmonization Guidelines.

RESULTS AND DISCUSSION

Selection of analytical wavelength

Selection of analytical wavelength is carried out by dividing absorption spectra of solutions at different concentrations using the sum of the absorption spectra of solutions of DMP+DPH (25 $\mu\text{g}/\text{mL}$ each in diluents), DPH+GUA (18 $\mu\text{g}/\text{mL}$ each in diluents), and GUA+DMP (12 $\mu\text{g}/\text{mL}$ each in diluents), respectively, for the determination of GUA, DMP, and DPH as double divisor to get the ratio spectra and their first derivatives were plotted with $\Delta\lambda$ 2 nm and scaling factor 1.0. The divided and derivatized spectra's (Figs. 1-3) showed maximum and minimum wavelengths. The wavelengths 280.0 nm, 286.1 nm, and 260.2 nm were selected for analysis of GUA, DMP, and DPH, respectively.

Method validation

The low values of percent relative standard deviation are indicative of the precision and reproducibility of the method. The resulting mixtures were assayed according to the above-stated procedure, and the results were calculated as the percentage of analyst recovered. LOD and LOQ values were indicated that the method shows high sensitivity. The good recovery values assure the high accuracy of the proposed method. Validation parameters for this method are shown in Table 1.

Based on Table 1, this research has good result validation method for simultaneous GUA, DMP, and DPH in their combine tablet dosage form.

Application of the method in commercial tablet

The proposed method was applied for the determination of GUA, DMP, and DPH in their combined commercial tablet and the results are shown in Table 2.

The results of analysis of pharmaceutical dosage form by the proposed method are in good agreement with label claim of the drug. According to this result, the proposed method is potential to use in routine drug analysis, especially drugs with contained the combination of several drugs. It is easy to work, especially for routine analysis and no require long conditioning tools.

CONCLUSION

The proposed method provides a simple, accurate, and precise quantitative analysis for the estimation of GUA, DMP, and DPH as a ternary mixture. The proposed method is simple as there is no need

for solvent extraction and direct as it estimates each component independent of the other, and also the method is rapid, low cost, and

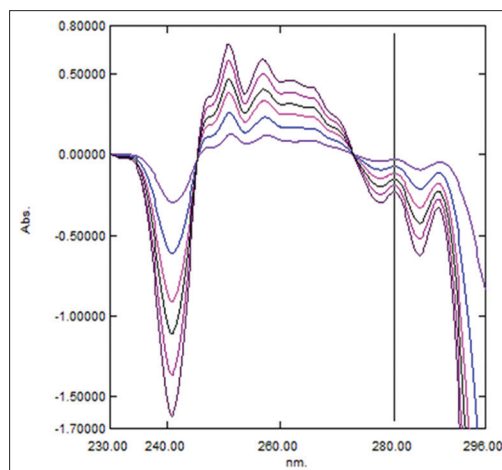


Fig. 1: Overlay first derivative ratio spectra of guaifenesin at 280.0 nm (DMP 25 $\mu\text{g}/\text{mL}$ +diphenhydramine hydrochloride 25 $\mu\text{g}/\text{mL}$ used as double divisor)

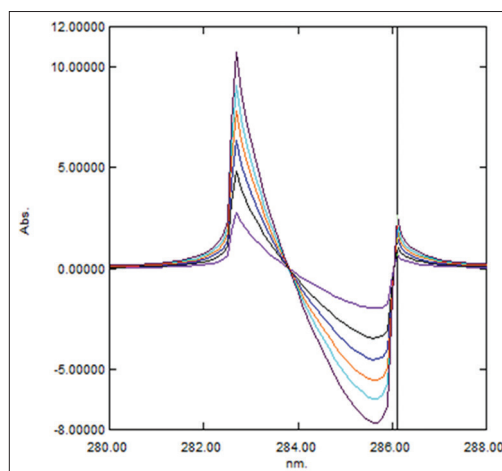


Fig. 2: Overlay first derivative ratio spectra of DMP at 286.1 nm (diphenhydramine hydrochloride 18 $\mu\text{g}/\text{mL}$ +guaifenesin 18 $\mu\text{g}/\text{mL}$ used as double divisor)

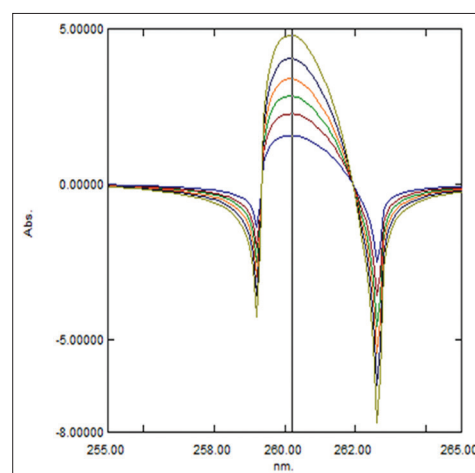


Fig. 3: Overlay first derivative ratio spectra of DMP at 260.2 nm (guaifenesin 12 $\mu\text{g}/\text{mL}$ +DMP 12 $\mu\text{g}/\text{mL}$ used as double divisor)

Table 1: Validation parameters for GUA, DMP, and DPH

| Parameters | GUA | DMP | DPH |
|--------------|--------|--------|--------|
| Accuracy (%) | 100.6 | 99.95 | 101.74 |
| Precision | 0.6422 | 0.6750 | 0.0254 |
| RSD (%) | | | |
| LOD | 1.5817 | 1.1671 | 1.1071 |
| LOQ | 4.7932 | 5.0630 | 3.3550 |

GUA: Guaifenesin, DPH: Diphenhydramine hydrochloride, RSD: Relative standard deviation, LOD: Limit of detection, LOQ: Limit of quantification, DMP: Dextromethorphan hydrobromide

Table 2: Result of quantification of GUA, DMP, and DPH in commercial tablet

| Commercial tablet | Drugs content | Amount found (mg/tablet) | Label claim (mg/tablet) |
|-------------------|---------------|--------------------------|-------------------------|
| Tablet L | GUA | 149.76 | 150 |
| | DMP | 9.99 | 10 |
| | DPH | 14.83 | 15 |

GUA: Guaifenesin, DPH: Diphenhydramine hydrochloride, DMP: Dextromethorphan hydrobromide

harmless to the environment. Hence, it could be applied in quality control laboratories.

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CONFLICT OF INTEREST

We declare that there is no conflict of interest.

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