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Original article

Development and validation of a simple method for the determination of triamcinolone acetonide in nasal spray

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ABSTRACT

A rapid, convenient, and sensitive analytical technique for quantitative analysis of triamcinolone acetonide (TAC) in pharmaceutical nasal spray dosage form using the blue tetrazolium colorimetric reaction and UV spectrophotometric method was developed and validated. Beer's law of the developed method was proven in the concentration range of 10–40 μg/mL and showed a specific linear relationship with coefficient value R2 = 0.998. The LOQ level was 9.99 μg/mL, with (RSD = 0.26%). From precision assay, RSD values have been obtained for the repeatability and intermediate precision, which were found to be (RSD = 1.65%) and (RSD = 2.01%), respectively, indicating that the method is reproducible. Recovery studies showed mean recoveries in the range of (100.08–103.65 %), meeting the acceptance criteria for accuracy. In addition, we compared the results of the developed method UV–Vis spectrophotometric procedure with those of a well-established official USP analytical procedure (HPLC), and the results showed good agreement. The proposed UV method represents a potential alternative to the official USP analytical assay procedure (HPLC) for estimating TAC in nasal spray forms. Furthermore, it has the potential to be implemented in routine use for rapid qualitative and quantitative determinations for TAC.

1. Introduction

Corticosteroids are a group of hormones synthesized and produced inside the adrenal glands. Corticosteroids, in general, play a pivotal role within the biological system, and the alternation of their levels can lead to detrimental disorders. There are two main classes of corticosteroids: glucocorticoids and mineralocorticoids. Glucocorticoids are stress hormones that play essential roles in the body and are responsible for immunosuppressive, anti-inflammatory, and vasoconstrictive effects, while mineralocorticoids regulate the electrolytes and water balance (Liu et al., 2013; Ramamoorthy & Cidlowski, 2016). Corticosteroids are therapeutically used to treat autoimmune, inflammatory diseases and cancer (Ericson-Neilsen & Kaye, 2014; Yasir et al., 2022). Importantly, inappropriate and prolonged use of corticosteroids can result in adverse side effects, such as non-healing of the wound, increased tension, weight gain, mood changes, high pressure, osteoporosis, and osteonecrosis (Yasir et al., 2022).

Corticosteroids exert their pharmacological effects through a complex mechanism of action involving reducing chronic inflammation and autoimmune reactions by encouraging the synthesis of specific anti-inflammatory proteins while inhibiting the synthesis of specific inflammatory mediators. As small lipophilic substances, glucocorticoids readily diffuse across the cell membrane into the cytoplasm of target cells, where most of their action is mediated by binding to specific intracytoplasmic glucocorticoid receptors of the target cells. Then, the corticosteroid-receptor complex translocates into the nucleus and influences the transcription of various genes involved in immune response and inflammation (Jeal and Faulds, 1997; Pitarokoili et al., 2019; Sons, 2023; Timmermans et al., 2019).

Triamcinolone acetonide (TAC) is an intermediate-acting synthetic glucocorticoid. In 2014, the U.S.Food and Drug Administration (FDA) authorized TAC as an over-the-counter (OTC) drug in the United States in nasal spray form (Fig. 1) (Narayan Nair, 2014).

By looking at the literature, several methods have been developed and reported for determining TAC in pharmaceutical dosage forms and matrices, as well as in biological fluids. Those works used different analytical methodologies and were mainly based on the physicochemical properties of TAC. In a previous study

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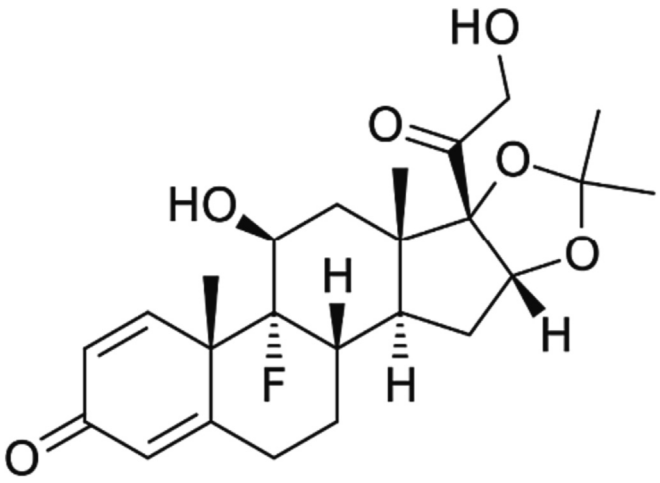

Fig. 1. Triamcinolone Acetonide chemical structure.

performed by (Wongman et al., 2021), a method was developed and validated to analyze the traced amount of TAC using ultra-performance liquid chromatography coupled with the photodiode array method (UPLC-PDA). TAC was successfully separated and quantified using the RP18 column with a gradient mobile phases system. The results were obtained in a short time with higher chromatographic performance. The method was capable of quantifying TAC in samples from skin permeation studies. Another study conducted by (Amendola et al., 2003) determined endogenous and synthetic glucocorticoids in human urine through gaschromatography–mass spectrometry (GC–MS) (quadrupole) with electron impact (EI) ionization and derivatization. The derivatizations were obtained by a two-step procedure under direct thermal heating and microwave (MW) irradiation, leading to high yields. The method was recommended to be a suitable analytical protocol for screening and confirmation in anti-doping tests. In addition, another study performed by (Singh & Verma, 2008) developed a sensitive method for determining steroids in pharmaceutical formulations (e.g., prednisolone, dexamethasone, prednisone, betamethasone sodium phosphate, and hydrocortisone) using a UV–Vis spectrophotometric protocol that was based on corticosteroid oxidation by iron with potassium hexacyanoferrate in an acidic medium, forming bluish green colored complex having the maximum absorbance at 780 nm. To that end, those reported methods required a long analysis time, and some necessitated extra steps, such as derivatization.

Blue Tetrazolium (BT) colorimetric reaction is an advantageous tool that can be used for analyzing corticosteroids. According to the previous studies that explained the mechanism of BT reaction with corticosteroids, BT acts as an oxidizing agent for the α-keto moiety on the C-17 side chain of the corticosteroid in strongly alkaline media. Mechanistically, an electron pair and a proton are transferred to BT from the anion formed, resulting in a colored formazan derivative product. Subsequently, the concentration of the resulting product for this colorimetric reaction can be measured by spectrophotometry (Amendola et al., 2003; Graham et al., 1975; Oteiza et al., 1977). Previously, a developmental study (Graham et al., 1978) that focused on the evaluation of different types of steroids (cortisone, cortisone acetate, dexamethasone, dihydrocortisone acetate, fluprednisolone, flurandrenolide, hydrocortisone, hydrocortisone acetate, prednisolone acetate, prednisone) has implemented the tetrazolium blue reaction in methylene chloride solvent. Results from that study were encouraging to further reproduce it on different types of corticosteroids.

One of the standard methods to analyze TAC is the official USP method according to (Daniel, 2013) for testing TAC in the nasal spray dosage form. However, this standard method is relatively high-cost, time-consuming, requiring about 50 min per run, and comprising many cumbersome preparation steps for the sample and mobile phase. That is considered an inconvenience, especially when conducting the performance test. The performance test is provided within the USP (Expert Committee of Chemical Medicines, 2019), which is divided into 2 stages. Firstly, the determination of delivered dose uniformity (between units). Secondly, calculations of distribution and delivery of dose uniformity (within the unit). Collectively, both performance tests require multiple samples and several injections. Moreover, this process would require over 24 h of running time and consume a large volume of the mobile phase. The need for an alternative method, which could possibly provide sensitive results in a short time, is highly desirable. Therefore, the need to develop a faster, handy, and uncomplicated procedure becomes demanded as literature data on this topic is scarce.

The current study aims to develop and validate a simple and fast method for TAC quantitation in nasal spray form using UV–vis spectrophotometry. In order to find the most efficient method conditions, several factors were studied and examined to optimize method parameters, including time, wavelength, and solvent.

2. Material and methods

2.1. Materials: Reagents and chemicals

Absolute ethanol (Honey well Riedel-de Haen. France)., methanol (Fisher chemical. UK), dichloromethane (DCM) (Merck. Germany), tetramethylammonium hydroxide (TMAH), and blue tetrazolium (BT) (TOKYO CHEMICAL INDUSTRY CO. LTD. JAPAN). Triamcinolone acetonide (TAC) reference standard is one corticosteroid ester selected for this study (USP Reference Standard Material). Fig. 1 shows the chemical structure of triamcinolone acetonide (TAC). The sample was obtained from the local market in the nasal spray form.

2.2. Instrument and software

The analysis was conducted using a Thermo Scientific Evolution 300 UV–Vis spectrophotometer with a 1 cm stoppered quartz cuvette. Data were collected using VISIO pro software and underwent analysis via Excel 2019.

2.3. Preparation of standard stock solution

A 100 μg/mL stock solution of triamcinolone acetonide standard (TAC) was prepared by dissolving the appropriate amounts (10 mg) in 100 mL of ethanol (Daniel, 2013). This standard stock solution of TAC was used for calibration curve preparation. For the calibration curve, different concentrations of analytical solutions were prepared by diluting the stock solution with the diluent dichloromethane (DCM) to analyze TAC. The selection of the DCM solvent and the reaction parameters were based on the work done by Graham et al with miner modification (Graham et al., 1978).

2.4. Preparation of reagents solution

Two solution reagents were prepared: a concentration of 5 mg/mL of blue tetrazolium (BT) in methanol and tetramethylammonium hydroxide (TMAH) was prepared in a 1:9 ratio in ethanol.

2.5. Sample extraction

For sample preparation and extraction, different concentrations were prepared based on the purpose needed for the method. A concentration of 20 μg/mL of the TAC sample was prepared in a suitable volume of DCM solvent to have the required final concentration. After that, the solution was thoroughly mixed via vortex for one minute. Then, it was placed in the centrifuge at 3000 rpm for 5 min for sample extraction. Finally, the clear liquid supernatant was collected.

2.6. Colorimetric reaction and spectrophotometric analysis

The colorimetric reaction of BT for TAC analysis was carried out in the ratio (1:1:10) of each reagent BT and TMAH to the targeted analyte TAC. The same colorimetric reaction was applied for the three volumetric flasks containing the sample, standard and blank, where a similar volume of DCM solvent serves as blank. Subsequently, the BT reagent was added and mixed. Later, the TMAH was added. Each reaction was mixed and kept for 5 min in the dark. After that, the absorbance result of the targeted analyte was measured at 525 nm wavelength against the blank (Fig. 2).

3. Method validation

The analytical method performance was validated following both the International Council for Harmonization (ICH) Q2 (R1) guidelines (Agency, 2020; Harron, 2013) and the USP-857. The validation has been done by evaluating the following parameters: specificity, linearity, limit of detection (LOD), limit of quantitation (LOQ), precision and accuracy of the method for the analysis of nasal spray containing triamcinolone acetonide (TAC).

3.1. Specificity

To assess the specificity of the method and to determine the optimum wavelength (λ max) of Triamcinolone Acetonide (TAC) analysis, the UV spectrum scans were performed in the range of 200–600 nm to evaluate possible overlap of absorption bands. The UV spectrum scans were performed for blank and the TAC standard reference before and after undergoing the colorimetric reaction with the BT reagent.

3.2. Linearity range and calibration curve

In order to evaluate the linearity, three independent standard calibration curves containing five concentration levels were prepared by diluting the known volumes of stock solution (100 μg / mL) with the DCM diluent to the mark and mixing well to get the required analyte concentrations into separate 25 mL volumetric flasks. TAC standard solutions were prepared in the range of 10–40 μg/mL (10, 15, 20, 30, 40 μg/mL). Triplicate measurement for each level was performed. The linearity was plotted between the known TAC concentrations (μg/mL) and its absorbance (UV– vis response). Statistically, the data were validated by analysis of variance (ANOVA). Also, the results obtained were used to calculate the linear regression equation (y = m × + c) using the linear Least–Least-squares regression method.

3.3. Limit of detection (LOD) and limit of quantification (LOQ)

The limits of detection (LOD) and quantification (LOQ) of triamcinolone acetonide were estimated directly from calibration curves, using the standard deviation from the error of the intercept and slope, as per the ICH guidelines (Agency, 2020; Harron, 2013).

$$\mathrm{LOQ} = 10\sigma/\mathrm{S}, \mathrm{LOD} = 3.3\sigma/\mathrm{S}.$$

Where σ is the standard deviation of the drug response, and S is the slope of the corresponding calibration curve.

3.4. Precision

Repeatability and intermediate precision were done to validate precision. The analyses were done in triplicate, and results were expressed as the analytical measurements' relative standard deviation (% RSD).

3.4.1. Repeatability (intra-day precision)

The repeatability was assessed by measuring the concentrations of six independently freshly prepared sample solutions of nasal spray at 10 μg/mL concentration on the same day and under identical experimental conditions.

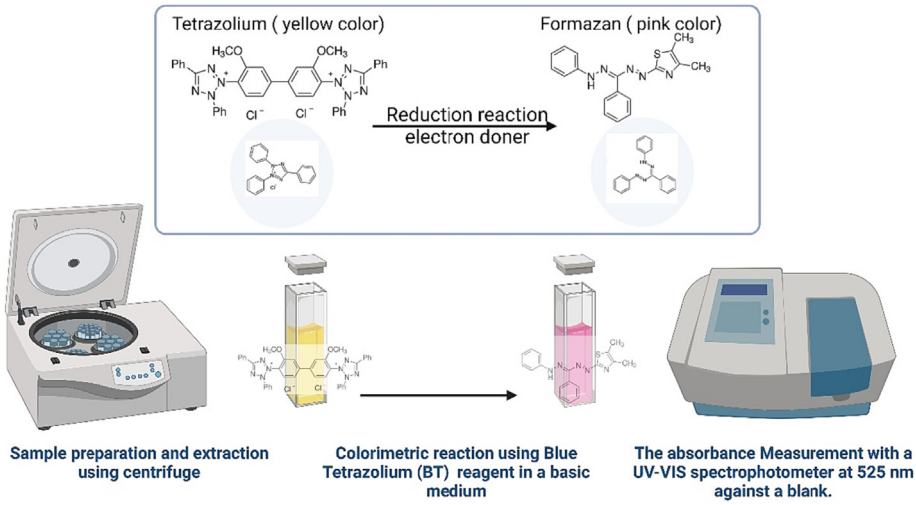

Fig. 2. Summary of the Colorimetric Reaction of Blue Tetrazolium (BT) for testing TAC using Spectrophotometric analysis: After the addition of the two reagents BT then TMAH, the color changed to pink-colored Formazan derivative, having the maximum absorbance at 525 nm. Determination of TAC that possess reducing functional groups such as alpha-ketols. The Tetrazolium Blue (BT) oxidizes the α-ketol moiety present in the C17 of corticosteroids in an alkaline medium, resulting in a highly colored formazan derivative. The figure Created with BioRender.com.

3.4.2. Intermediate (Inter-day Precision)

The intermediate precision was determined by comparing the sequential repeatability analysis on different days by assaying freshly prepared samples of nasal spray.

3.5. Accuracy

Accuracy was determined by conducting a recovery test, considering the suitable matrix spiked with known concentrations of the analyte to confirm the absence of a matrix effect. The test was carried out by adding known amounts of the standard reference solution to the sample at different concentration levels (10, 14, 18, 20 μg/mL). Triplicate measurement for each level was performed. Subsequently, the total drug content in the final matrix was analyzed. The recovery study results are expressed as a percentage of the drug recovered.

4. Results

4.1. Preliminary tests for method development: Optimization of different reaction variables

The method development started with several preliminary experiments to determine the best conditions for the method analysis. Based on the UV spectrum scan results shown in Fig. 3, the maximum absorption wavelength was 525 nm. Next, the effect of different solvents was tested against the reaction rate and efficiency. Based on our preliminary results, we focused on investigating two solvents, DCM and ethanol, distinguished by their rapid reaction rate and high efficiency as per our study goals. It has been demonstrated that the oxidation reaction of the α-keto group of TAC in DCM solvent could be carried out in 5 min as opposed to 90 min when ethanol was used as a reaction solvent (Fig. 4). However, the absorbance continued for 120 min. Moreover, the formazan product was stable for over 90 min **(**Fig. 3 **and** Fig. 4**).**

4.2. Specificity

4.2.1. Determination of λ max

Specificity was assessed by comparing the UV spectra scans. The results of UV spectrum scans indicated the maximum absorbance of formazan product at 525 nm due to the adequate molar absorptivity and the higher selectivity of this wavelength regarding possible interfering compounds or solvents in the samples. So, the analysis has demonstrated selective and specific characteristics of the targeted analyte. Representative UV spectra of the TAC standard undergoing the colorimetric reaction with the reagents are presented in Fig. 5(A, B, and C). Fig. 5(A) shows the maximum absorbance of TAC around 230 nm, which agrees with the previous analytical data that reported that the UV spectrum λ max at 238 nm (Iwata et al., 1999). At the wavelength of around 230 nm, it was possible to observe an interference because most chemicals can be absorbed in this range.

For this reason, we resorted to the colorimetric reactions that help enhance the result's fineness and avoid interference with the results. The optimum wavelength of the TAC analysis using BT colorimetric reaction was identified at 525 nm Fig. 5(C). Practically, this performance elucidated that there was no interference in the analysis. Collectively, it was concluded that the method fulfilled the selectivity and specificity criteria for the study of TAC at the maximum absorbance of formazan product at 525 nm.

4.3. Linearity and range results (Calibration Curve)

Linearity regression results were obtained under the optimum experimental conditions, as summarized in Table 1. The standard calibration curve of TAC in the DCM solvent showed a good linearity in the range of (10–40 μg /mL) with the coefficient value R^2 = 0.998, indicating a linear relationship. Table 2**.** shows the regression analysis and the ANOVA of the standard calibration curve of TAC. ANOVA test demonstrated a significant linear regression ($p < 0.05$). Successfully, statistical analysis by ANOVA confirmed the linear regression. The statistical *p*-value obtained (0.025) indicated a significant statistical difference from zero point in the calibration range worked at the 95% confidence level.

4.4. Limit of detection (LOD) and limit of quantification (LOQ)

4.4.1. LOD and LOQ determination from calibration curves

The estimated LOD and LOQ of TAC from standard calibration curves were 3.091 μg/mL and 9.368 μg/mL, respectively. The estimated results indicated that the sensitivity of the proposed UV method was suitable for TAC analysis. Also, LOQ was validated by further determination of TAC in actual pharmaceutical samples. The LOD level for TAC confirmed that the method could detect TAC levels in the validated range, where the practical LOD value corresponded to the estimated value.

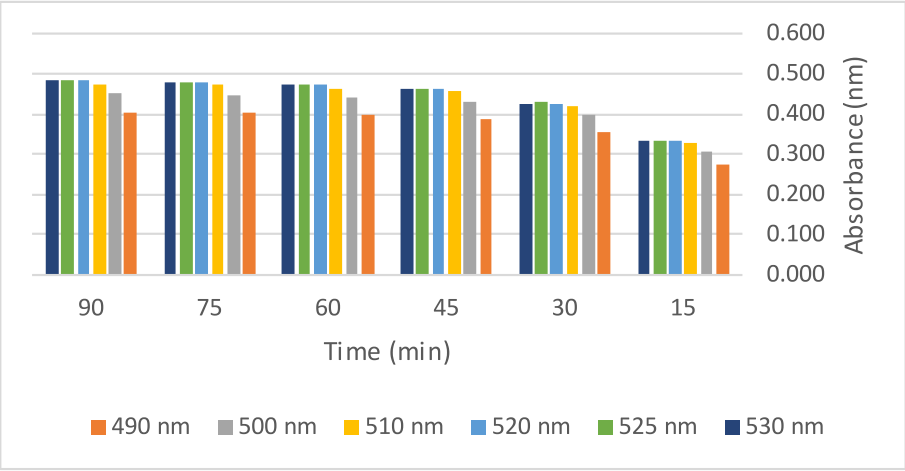

Fig. 3. Triamcinolone Acetonide (TAC): scan multi-wavelength absorption vs. time.

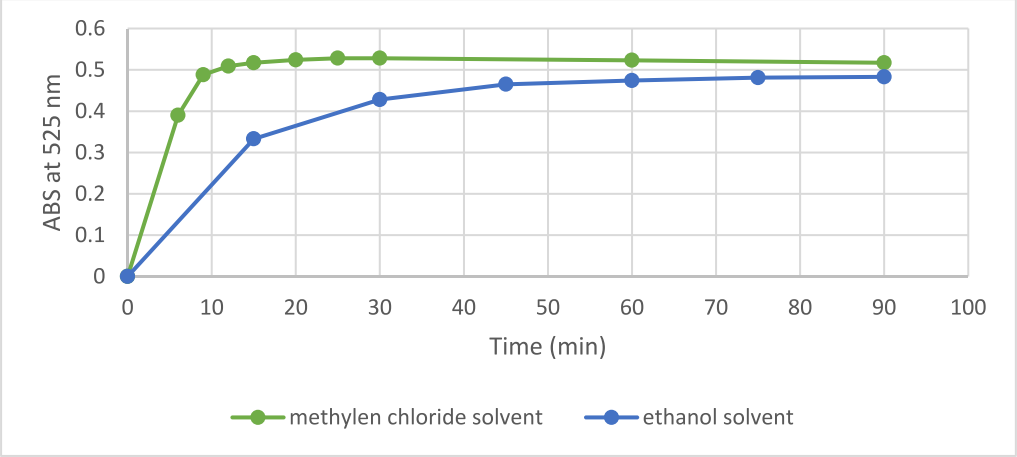

Fig. 4. Time vs. Absorbance graph for Triamcinolone Acetonide (TAC) (green: DCM solvent, Blue: ethanol solvent).

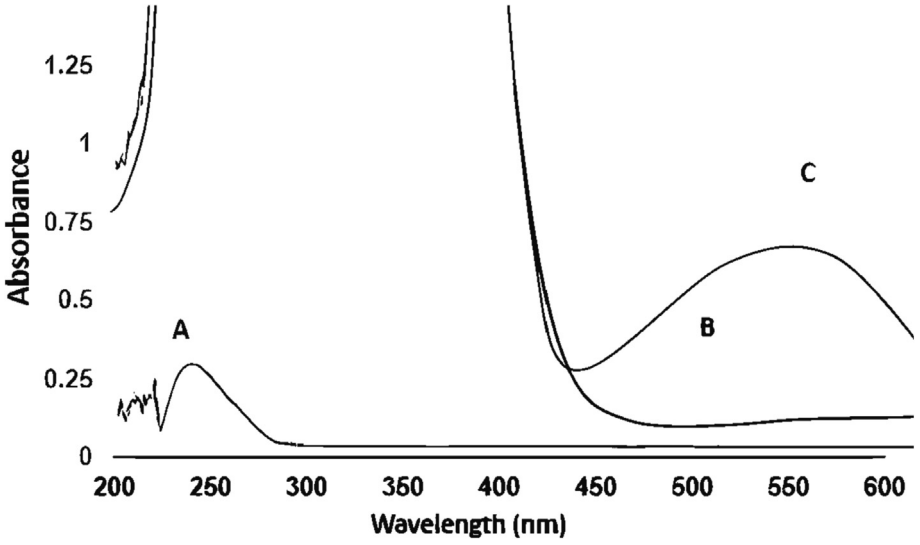

Fig. 5. UV–Vis absorption Scan spectra within the range of 200–600 nm wavelength: (A) 10 ppm Triamcinolone acetonide standard solution (B) Reagents (BT and TMAH), (C) Colorimetric reaction of TAC Standard with the reagents.

Table 1
Linear Regression results obtained from validation of UV spectrophotometric obtained from validation of UV spectrophotometric method for quantitative determination of Triamcinolone Acetonide (TAC) in nasal spray.

Analyte	Triamcinolone Acetonide (TAC)
Linearity range	(10–40 µg /mL)
Analytical wavelength λ max (nm)	525 nm
Regression equation	y = 0.0368x + 0.088
Selected fit	linear
Slope	0.0367
Intercept	0.0879
Sum of residual	0.0239
Validation Acceptance criteria	The coefficient of determination, r2, must be NLT 0.995 for Category I assays
Correlation coefficient (R2)	R^2 = 0.998
Conclusion	Criteria met. Linearity confirmed.

4.4.2. Validation of LOQ from spiked recovery experiments

LOQ was studied by analyzing a series of ten replicate measurements of a sample solution prepared from a representative sample matrix at a specific concentration (10 µg/mL). Consequently, the required LOQ concentration of TAC could be quantitated with acceptable precision and accuracy under the stated experimental conditions. Evidently, the LOQ level was found to be 9.99 µg/mL, which met the acceptance criteria of the LOQ. The LOQ data is presented in Table 3.

4.5. Precision

The precision parameter for the developed method was assessed, and the obtained results are demonstrated in Table 3 for the repeatability (intra-day precision) and intermediate (Inter-day precision), respectively. The %RSD values met the acceptance criterion and showed that the UV spectrophotometric methods exhibited good Intra and Inter-day precision.

4.6. Accuracy

The proposed UV spectrophotometric method in this study showed good accuracy for quantitating TAC in nasal spray pharmaceutical form. Table 4 shows the result of the recovery study, presenting an average recovery within the range of (100.08–103.65 %). The recovery results met the acceptance criteria of accuracy.

Table 2
The regression analysis and the ANOVA of TAC calibration.

Regression Statistics								
Multiple R	0.999							
R Square	0.998							
Adjusted R Square	0.997							
Standard Error	0.020							
Observations	5							
ANOVA								
	df	SS	MS	F	Significance F			
Regression	1	0.784	0.784	1942.284	2.57E-05			
Residual	3	0.0012	0.0004					
Total	4	0.7855						
	Coefficients	Standard Error	t Stat	P-value	Lower 95%	Upper 95%	Lower 95.0%	Upper 95.0%
Intercept	0.0879	0.0211	4.1526	0.02538	0.0205	0.1554	0.02056	0.1554
Conc (μg/ml)	0.0367	0.00083	44.071	2.57E-05	0.0341	0.0394	0.0341	0.0394

Table 3
Summary of validation parameters.

Validation Parameters	**Result**	**Validation Acceptance criteria**
Linearity (Range) (R2)	(10–40 μg / mL) (R^2 = 0.998)	The coefficient of determination, R^2, must be NLT 0.995 for Category I assays
Limit of Detection (LOD) μg/mL	3.091 μg/mL	The smallest measure of analyte that can be detected with reasonable certainty for a given analytical procedure
Limit of Quantitation (LOQ) (Mean Conc μg/mL) (% RSD)* LOQ Measurements with Respect to The Theoretical Concentration Of (10 μg/mL). *For Ten Replicates, N = 10	(9.982 μg/mL), (0.264%)	The measured concentration must be accurate and precise at a level ≤ 50%
Accuracy (Mean % Recovery)	102.17%	95.0%–105.0% mean recovery for the drug product assay
Repeatability (Intra-Day Precision) (%RSD)	(1.65%)	The relative standard deviation is NMT 2.0% for the drug product assay.

Table 4
Results of recovery studies for validation of UV spectrophotometric methods for quantitation of Triamcinolone Acetonide in nasal spray.

	Theoretical concentration (μg/mL)	Actual Concentration (μg/mL)	Recovery %
Level 1	15.72	16.28	**103.56**
Level 2	19.72	20.44	**103.65**
Level 3	23.72	24.05	**101.39**
Level 4	25.72	26.00	**100.08**
Mean % Recovery	102.17%		

5. Discussion

In the current study, we developed and validated a simple and fast method for TAC quantitation in nasal spray pharmaceutical form using UV–vis spectrophotometry. The developed validated UV–vis spectrophotometry method showed significant advantages.

During the method development stage, the wavelength 525 nm was selected, which in practice did not demonstrate any interferences, as shown in the results section. This observation is in agreement with the USP procedure as well as published research (Daniel, 2013; Graham et al., 1978; Kumar & Kamboj, 2020) that indicated that the maximum absorption wavelength of formazan was at 525 nm after scanning pink-colored formazan from 200 to 600 nm.

Mechanistically, the reaction of alpha ketol and formazan is governed by multifaceted factors, such as pH, solvent, water, temperature and steric hindrance (Graham et al., 1975, 1978; Mader & Buck, 1952). Concerning solvent selection, the official USP (Daniel, 2013) procedure utilizes ethanol as a solvent, which specifies the analytical protocol for the reaction to be conducted in the dark for 90 min. However, after trying ethanol and DCM in the current study, we found that using DCM as a reaction's solvent enhanced the efficiency of the reaction's response in a shorter time (Fig. 4). In fact, our results showed that DCM increased reaction rate and color development by as fast as 5 min. Furthermore, the procedure is still quantitative, specific, and qualitative despite shortening the reaction time. It seems that the advantages of DCM for providing rapid and stable formazan complex are attributed to its lower polarity feature compared to alcohol. Indeed, a previous work by (Graham et al., 1978) has demonstrated that DCM and chloroform-related reaction rate was more than six times faster as compared to a polar solvent, such as an alcohol.

As depicted in Fig. 6, a primary comparative study was conducted between two methods, namely the USP analytical assay procedure HPLC and the UV–Vis spectrophotometry, in order to analyze the accuracy further. The samples were prepared in triplicate, and concentration results were compared utilizing statistical analysis, with the p-value serving as a measure of significance (p-

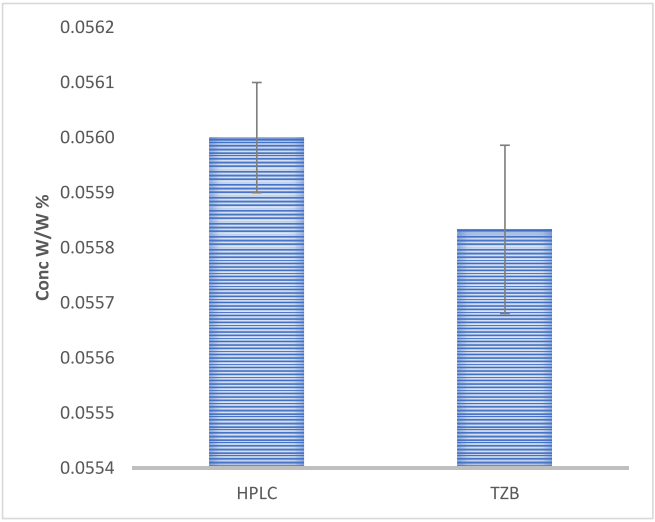

Fig. 6. The assay results of TAC were obtained using the UV–Vis procedure, compared to the assay results from an official USP analytical procedure (HPLC).

value = 0.1). The results indicated no significant difference between the outcomes obtained from the two methods, thereby demonstrating their agreement. These findings support the hypothesis that the UV–Vis spectrophotometry procedure has the potential to serve as an alternative method to the official USP analytical assay procedure (HPLC) for estimating TAC in nasal spray form. This is supported by the satisfactory validation results obtained for the UV–Vis spectrophotometry method and the assumption that the procedure HPLC's validated status. It is worth noting that the developed method showcases a more rapid and less complicated approach.

Another variable factor that may impact the reaction rate is the temperature. A previous research (Amin, 2001) demonstrated the effect of heating on the speed of the oxidation–reduction reaction compared to the room temperature. Their results showed that the response can be shortened from 3.0 h to 10 min by raising the temperature to 90 °C, where a highly colored formazan derivative is produced within 10 min. A previous study (Scremin et al., 2010) aimed to validate and compare three different techniques, namely UV spectrophotometry, colorimetric approach with blue tetrazolium and HPLC method, to study the stability for one glucocorticoid called deflazacort in tablets and oral suspension forms. The results indicated that the UV and HPLC methods were statistically equivalent. In contrast, the colorimetric method with blue tetrazolium differed significantly. Nevertheless, the results from that study are not evidently relevant to our study owing to the distinct factors, particularly formazan reaction conditions and the identity of the corticosteroid used in the earlier study.

During the early steps of the method development, we attempted several corticosteroids to explore the potential of the method. Also, we investigated a few pharmaceutical formulations and realized that the experimental conditions might vary depending on the type of functional group attached to the corticosteroids. As a result, this work paves the road to investigate the versatility of BT reagents for other potential applications relevant to the method's scope. In addition, the low number of real samples is considered a limitation of the current work, and hence, further work can be conducted utilizing a larger sample size to enhance the statistical robustness of the new method.

6. Conclusion

The current study demonstrated the proof of concept of developing an alternative approach for the assay of TAC in pharmaceutical nasal spray dosage form. The newly developed method possesses numerous advantages, such as one-step sample extraction without needing pH or temperature control, low chemical-waste generation, less analysis time, and low operation costs. Consequently, this developed method is recommended for routine quality control analysis. Nevertheless, additional optimization and large-scale sample analysis are needed to confirm its comparability to the compendial analytical method. Considering the time and effort savings, the presented method would be a promising approach for the rapid detection of corticosteroids both quantitatively and qualitatively.

7. Disclaimer

"The views expressed in this are those of the author(s) and not do not necessarily reflect those of the SFDA or its paper stakeholders. Guaranteeing the accuracy and the validity of the data is the sole responsibility of the research team".

CRediT authorship contribution statement

Haya S. Alzeer: Investigation, Data curation, Formal analysis, Methodology, Validation, Visualization, Writing - original draft, Writing - review & editing. **Shikah F. Alzaid:** Validation, Investigation, Methodology, Writing - original draft. **Fahad S. Aldawsari:** Supervision, Investigation, Conceptualization, Writing - review & editing. **Yahya M. Alshehri:** Conceptualization, Supervision, Investigation, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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