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A validated, stability-indicating HPLC method for the determination of dexamethasone related substances on dexamethasone-coated drug-eluting stents

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ABSTRACT

An HPLC method was developed and validated to determine trace amounts of dexamethasone related substances on dexamethasone-coated drug-eluting stents. Separation of dexamethasone from its major process impurities and degradation products was achieved on a Zorbax Eclipse XDB C8 column using gradient elution and UV detection at 239 nm. The method was validated according to ICH guideline requirements. In addition, stent extraction efficiency, solution stability and method robustness were evaluated.

The method was determined to be linear in the range of 0.01–0.30 μg ml^{-1} for the quantitation of major dexamethasone related substances. Method accuracy was assessed by spiking dexamethasone acetate at three levels over the range of 0.025–0.175 μg ml^{-1}. The dexamethasone acetate recovery ranged from 89.6 to 105.8%. The intermediate precision over the three levels was less than 6% ($n = 9$). The method was also shown to be repeatable at concentration levels of 0.025, 0.125 and 0.175 μg ml^{-1} dexamethasone with relative standard deviation values of 4.1, 1.7 and 1.6%, respectively. The method was found to be specific, stability-indicating, and sensitive with a detection limit of 0.008 μg ml^{-1} and a quantitation limit of 0.025 μg ml^{-1} dexamethasone. Finally, the method was demonstrated to be robust, resistant to small variations of chromatographic variables such as pH, mobile phase organic/aqueous composition and column temperature.

Identifying unknown dexamethasone degradation products in dexamethasone-coated drug-eluting stents was of critical interest to ensure product quality, since degradants have a significant impact on safety, efficacy, and product storage and handling. The developed chromatographic method was designed to be compatible with mass spectrometric detection. This paper also discusses using this chromatographic method coupled to an ion-trap LCQ mass spectrometer to elucidate proposed structures for four major dexamethasone degradants.

1. Introduction

Dexamethasone, a potent synthetic corticosteroid with anti-inflammatory and immunosuppressive properties, is frequently used as an anti-inflammatory agent [1]. It has been widely used to treat inflammation, allergy and diseases related to adrenal cortex insufficiency. Dexamethasone is also known to reduce neointimal hyperplasia in arteries [2] and has been used for coating drug-eluting stents for local drug delivery to prevent restenosis [3–5], for example, Dexamet™ (Abbott Vascular Devices Ltd.). Dexamet™, the coronary stent coated with phosphorylcholine (PC) polymer and dexamethasone.

High-performance liquid chromatography (HPLC) is a powerful tool to analyze complex samples, such as drug-coated stents and tissue samples, since it can provide separation from impurities and eliminate interferences from a complex matrix. Several HPLC methods have been reported in the literature describing the analysis of dexamethasone and its related substances using UV detection [6–8]. HPLC separation and quantitation methods for dexamethasone and related substances can also be found in Compendia, such as monographs in USP 30-NF 25 [9], European Pharmacopeia 5.0 [10] and Japanese Pharmacopeia XIV [11]. All of these methods were used to quantify dexamethasone and degradants in plasma and tissue samples or used for specific dexamethasone injections and

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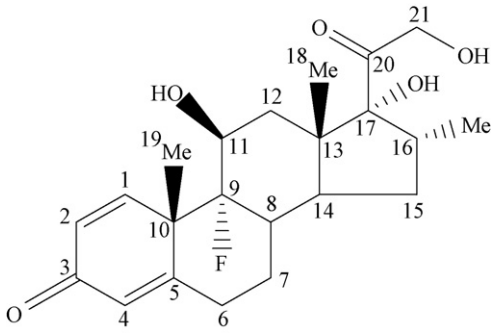

Fig. 1. Chemical structure of dexamethasone.

dexamethasone drug substances. None of these methods can meet the current regulatory requirements for analyzing low level dexamethasone related substances (e.g., ng ml^{-1} level) on drug-eluting stent products. An improved method for the determination of dexamethasone related substances is needed to meet this demand.

Dexamethasone has the chemical name 9-fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione and molecular formula $C_{22}H_{29}FO_5$ (Fig. 1). The chemical stability of dexamethasone is relatively high, however, several potential synthetic impurities, degradation products and metabolites have been reported in the literature [12,13]. The primary goal of this study was to develop and validate an HPLC method that could separate dexamethasone from its potential related substances and has sufficient sensitivity for quantitation of these impurities at very low concentrations. Degradation products formed from dexamethasone subjected to forced-degradation conditions, such as acid, base, heat, light and oxidation treatment, were investigated using HPLC, LC/MS and LC/MS/MS techniques. The structures of degradation products are proposed in this article.

2. Experimental

2.1. Materials and reagents

All aqueous solutions including the HPLC mobile phase were prepared with in-house purified water. HPLC grade acetonitrile was obtained from Burdick and Jackson (Muskegon, MI). Ammonium formate was purchased from Fluka (Sigma–Aldrich, Chemie GmbH, Switzerland) and formic acid was obtained from J.T. Baker (Phillipsburg, NJ). Absolute ethanol was purchased from Aaper (Shelbyville,

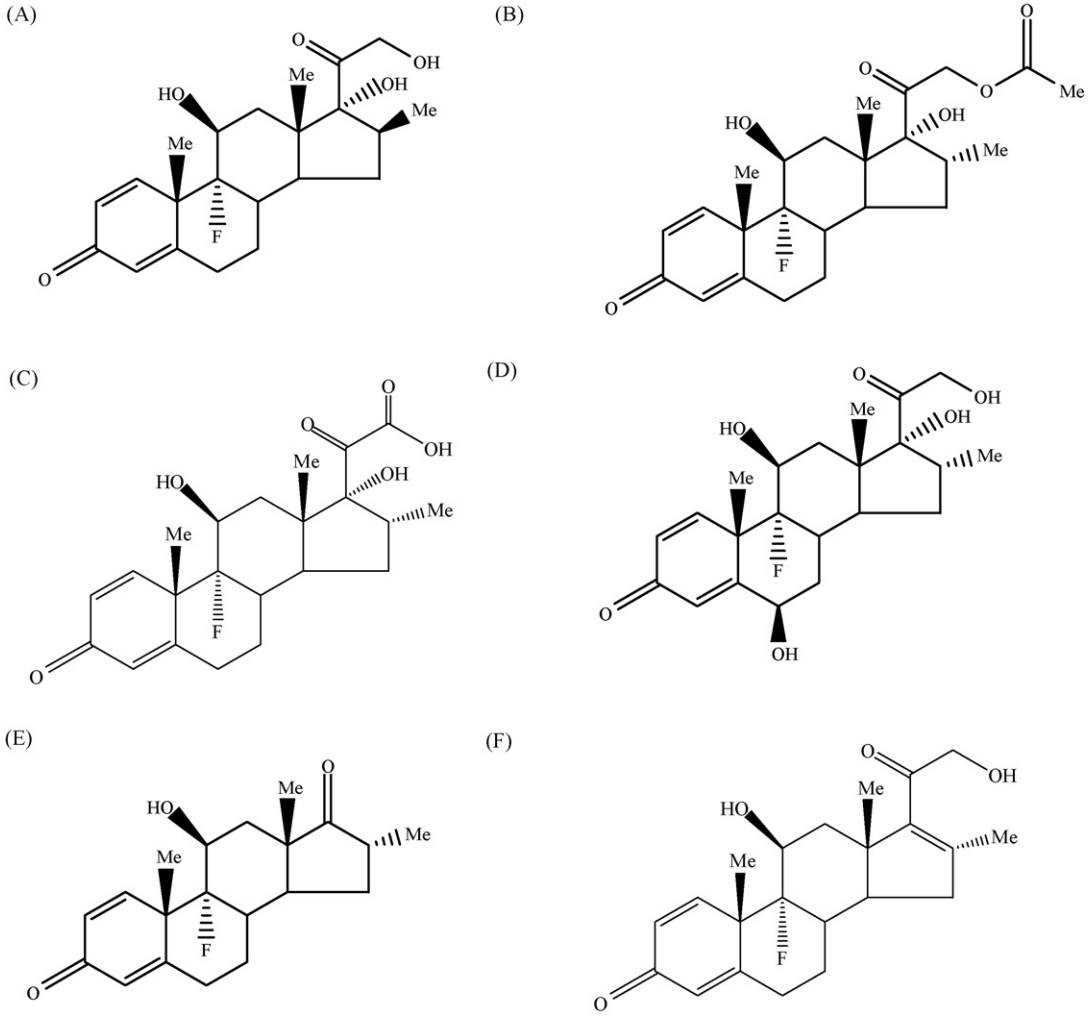

Fig. 2. Chemical structures of dexamethasone process impurities and degradation products. (A) Betamethasone: process impurity; (B) dexamethasone acetate: process impurity; (C) dexamethasone-21-oic acid: degradation product with MW 406; (D) 6β-hydroxydexamethasone: degradation product with MW 408; (E) 17-oxodexamethasone: degradation product with MW 332; (F) 16,17-unsaturated dexamethasone: degradation product with MW 374.

Table 1
Typical results from the determination of system suitability

Parameter	Criteria	Results
Dexamethasone retention time (Dex RT)	10–15 min	12.92
Resolution (R)	≥10.0	15.7
Tailing factor (T)	≤1.5	1.2
Number of theoretical plates (N)	>5000	8678
Injection repeatability for working standard (R.S.D., $n=6$)	≤5.0% ($n=6$)	0.2
Retention time repeatability for working standard (R.S.D., $n=6$)	≤2.0% ($n=6$)	0.1
Ratio of working standard and limit of quantitation standard (standard ratio)	4.0–6.0	5.1

KY). Methylparaben was an internal Abbott standard and used as a resolution solution component. Dexamethasone USP was obtained from U.S. Pharmacopeia (Rockville, MD) and used as the reference standard in the HPLC analysis. Dexamethasone drug substance was obtained from Aventis (Woodcliff Lake, NJ). Betamethasone and dexamethasone acetate were purchased from Sigma–Aldrich (St. Louis, MO). Dexamethasone-coated stents are prototype drug-eluting stents obtained from Abbott Vascular Devices (Redwood City, CA).

2.2. HPLC and conditions

Agilent 1100 series HPLCs with either a variable-wavelength detector or a multi-wavelength photodiode array detector (PDA) were used for the work. The typical HPLC system consisted of a G1322A model degasser, G1311A model pump, G1329A model autosampler equipped with 1400 μl Multidraw upgrade kit, G1316A model HPLC column compartment and G1314A model UV detector (variable wavelength), or G1315A model PDA detector. Chromatographic data were acquired and processed using the Atlas 2003R1 data acquisition system (Thermo Electron Corp.). Chromatographic separations were performed on a Zorbax (Agilent Technologies, U.S.A.) Eclipse XDB-C8 column (4.6 mm × 250 mm, 5 μm particle size). The separation was achieved with a gradient program consisting of 0–12 min 100% mobile phase A (mixture of a buffer comprised of 20 mM ammonium formate with the pH adjusted to 3.8 with formic acid and acetonitrile in a 73:27 (v/v) ratio) and 12–40 min gradient up to 45% mobile phase B (100% acetonitrile). After 40 min the gradient was returned to the initial conditions and the analytical column was reconditioned for 10 min. The flow rate was maintained at 1.5 ml min^{-1} with UV detection at 239 nm. The sample injection volume was 250 μl and the column temperature was maintained at 45 °C.

2.3. Liquid chromatography–mass spectrometry (LC/MS)

The LC/MS studies for impurity identification were carried out on a LCQ ion-trap LC–MS system (ThermoFinnigan, U.S.A.) coupled with an Agilent 1100 series HPLC. The HPLC was composed of a quaternary pump, degasser, autosampler, and column oven as described in Section 2.2. The chromatographic conditions were identical to that described above. The HPLC effluent was introduced into ion-trap by the electrospray ionization (ESI) source of the LCQ mass spectrometer for analysis. MS data were acquired in positive ion mode. The capillary voltage was set at 4.5 kV. The capillary source temperature was set at 250 °C. Nitrogen was used as sheath and auxiliary gas. The range of m/z acquired was from 150 to 1000.

2.4. Sample preparation

Prototype stents of two different sizes (2.5 mm × 13 mm and 3.0 mm × 13 mm with target 10 μg mm^{-1} of dexamethasone) were evaluated. For sample preparation, one stent was transferred into a clean and dry amber vial and extracted with 3.0 ml of a mixture of ethanol and the pH 3.8 formate buffer (50:50, v/v) for 40 min. Then 3.0 ml of a mixture of the pH 3.8 formate buffer and acetonitrile (70:30, v/v) was added to the vial and mixed. An aliquot was transferred to injection vials for HPLC analysis.

3. Results and discussion

3.1. Method development and optimization

The chemical structure of dexamethasone is shown in Fig. 1 and the proposed chemical structures of major dexamethasone process and degradation related substances are shown in Fig. 2.

Table 2
Results from the determination of accuracy of the method

Impurity/media	Level (%)	Concentration (μg ml^{-1})		Recovery (%)	R.S.D. ($n=3$ (%))	R.S.D. ($n=9$ (%))
		Added	Recovered			
Dex acetate/liquid formulation	0.1	0.0260	0.0242	93.1		
	0.1	0.0260	0.0233	89.6		
	0.1	0.0260	0.0245	94.2	2.6	
	0.5	0.1299	0.1235	95.1		
	0.5	0.1299	0.1235	95.1		
	0.5	0.1299	0.1266	97.5	1.4	
	0.7	0.1819	0.1736	95.4		
	0.7	0.1819	0.1743	95.8		
	0.7	0.1819	0.1740	95.7	0.2	2.4
Dex acetate/coupon	0.1	0.0260	0.0241	92.7		
	0.1	0.0260	0.0275	105.8		
	0.1	0.0260	0.0272	104.6	7.2	
	0.5	0.1299	0.1166	89.8		
	0.5	0.1299	0.1191	91.7		
	0.5	0.1299	0.1308	100.7	6.2	
	0.7	0.1819	0.1713	94.2		
	0.7	0.1819	0.1765	97.0		
	0.7	0.1819	0.1773	97.5	1.8	5.8

Table 3
Intermediate precision of dexamethasone acetate

Level (%)	Analyst	Concentration ($\mu g\,ml^{-1}$)		Recovery (%)	R.S.D. ($n = 6$ (%))
		Added	Recovered		
0.1	1	0.0260	0.0242	93.1	
0.1	1	0.0260	0.0227	87.3	
0.1	1	0.0260	0.0227	87.3	
0.1	2	0.0260	0.0252	96.9	
0.1	2	0.0260	0.0239	91.9	
0.1	2	0.0260	0.0244	93.8	4.1
0.5	1	0.1299	0.1235	95.1	
0.5	1	0.1299	0.1234	95.0	
0.5	1	0.1299	0.1200	92.4	
0.5	2	0.1299	0.1247	96.0	
0.5	2	0.1299	0.1253	96.5	
0.5	2	0.1299	0.1258	96.8	1.7
0.7	1	0.1819	0.1736	95.4	
0.7	1	0.1819	0.1726	94.9	
0.7	1	0.1819	0.1685	92.6	
0.7	2	0.1819	0.1746	96.0	
0.7	2	0.1819	0.1730	95.1	
0.7	2	0.1819	0.1768	97.2	1.6

The US Pharmacopeia (USP 30-NF 25) specifies a method for HPLC determination of dexamethasone and related impurities using 254 nm detection and a mobile phase containing 670 ml of pH 3.6 formate buffer and 330 ml of acetonitrile with a flow rate of 1.0 ml min^{-1}. When using HPLC conditions delineated in the USP, we found that late-eluting species, such as 17-oxodexamethasone and dehydrated dexamethasone, had broadened peak shapes resulting in sensitivity loss. The method was also less sensitive since detection wavelength was not the UV absorption maximum for dexamethasone in this medium.

The Japanese Pharmacopeia (JP XIV) has a similar HPLC method using isocratic mobile phase of water and acetonitrile (2:1, v/v) with UV detection at 254 nm. With JP conditions, we experienced similar problems as we did with the USP method.

The European Pharmacopeia 5.0 specifies an HPLC method for the determination of dexamethasone related substances using 254 nm detection and gradient program of mobile phase A (250 ml of acetonitrile and 750 ml of water) and mobile phase B (acetonitrile) with a flow rate of 2.5 ml min^{-1}. With EP HPLC conditions, the HPLC baseline was not ideal and late-eluting related substances, 17-oxodexamethasone and dehydrated dexamethasone, had poor peak shapes in the gradient elution region. Due to UV detection at 254 nm, the method was also not sensitive enough for the detection and quantitation of low level impurities.

Therefore, it was necessary to change several HPLC variables. The optimal detection wavelength was chosen at 239 nm since it is the wavelength of maximum UV absorbance for dexamethasone in the chosen mobile phase. A buffer of 20 mM ammonium formate with a pH adjusted to 3.8 with formic acid was used to achieve stable baseline and better peak shapes. The mobile phase gradient program was optimized as mentioned in Section 2.2. The flow rate was finalized at 1.5 ml min^{-1}. The chromatographic separation was achieved on a Zorbax Eclipse XDB C8, 250 mm × 4.6 mm, 5 μm column maintained at 45 °C.

3.2. Method validation

The method was validated according to International Conference on Harmonization (ICH) Q2 (R1) requirements [15]. The following validation parameters were addressed: linearity, range, accuracy, precision, specificity and stability-indication, limit of detection, limit of quantitation, stent extraction efficiency, solution stability and robustness.

3.2.1. System suitability

System suitability tests were performed to ensure that the HPLC system and procedure are capable of providing quality data based on USP 30 requirements. Resolution solution (solution of dexamethasone and methylparaben), dexamethasone limit of quantitation standard (0.025 $\mu g\,ml^{-1}$) and a bracketing working standard (0.125 $\mu g\,ml^{-1}$) were injected in each HPLC run. The system suitability parameters include dexamethasone retention time, tailing factor, resolution and number of theoretical plates, as well as the retention time and peak area relative-standard deviation (R.S.D., $n = 6$) of bracketing working standards. The peak area ratio of working standard vs. limit of quantitation standard was also required as part of the system suitability assessment. Table 1 lists the system suitability criteria and representative test values.

3.2.2. Linearity and range

The linearity of dexamethasone and two process impurities, betamethasone and dexamethasone acetate, were evaluated at eight concentrations in the range of 0.01–0.30 $\mu g\,ml^{-1}$. This range corresponds to impurity levels of 0.03–1.2% (w/w) of the active pharmaceutical ingredient (API) in stent samples. The linearity curves were defined by the following equations

$$y = 381.8858x + 0.0038,\ r = 1.0000 \text{ for dexamethasone}$$

$$y = 375.5409x + 0.0082,\ r = 1.0000 \text{ for betamethasone}$$

Table 4
Stress conditions for dexamethasone solution samples

Stress condition	Solvent	Stress treatment
Acidic	20% ethanol, 80% 0.01N HCl	0.01N HCl, 105 °C, 16 h
Basic	20% ethanol, 80% 0.01N NaOH	0.01N NaOH, 105 °C, 16 h
Oxidative	20% ethanol, 80% 4.8% H_2O_2	30% H_2O_2, room temperature, 1 day
Thermal	20% ethanol, 80% H_2O	105 °C, 16 h
Light	20% ethanol, 80% H_2O	Cool white fluorescent light for 24 h and UV light for 1 h

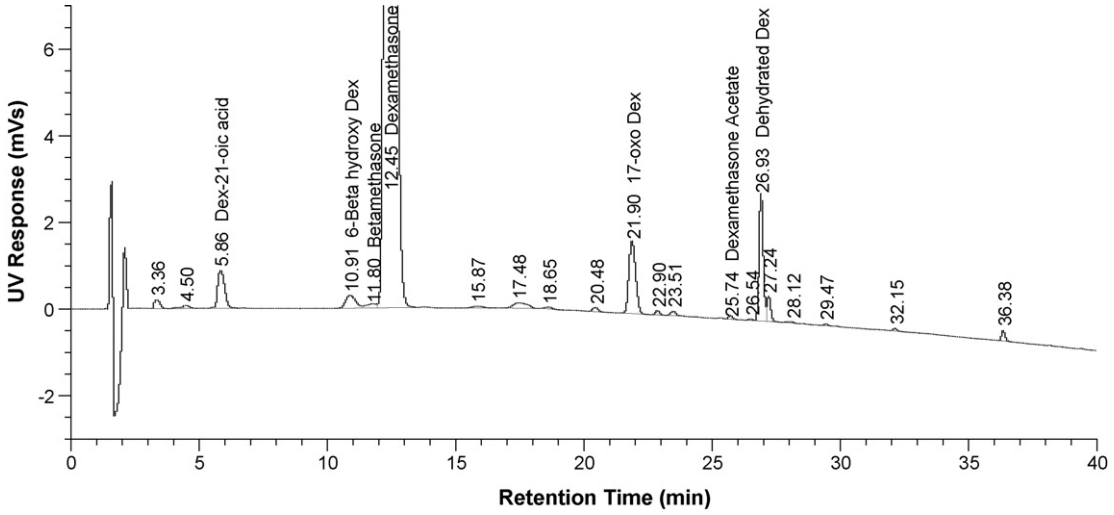

Fig. 3. HPLC chromatogram of thermally degraded dexamethasone 25 μg ml^{-1}.

$$y = 349.0064x - 0.2686,\ r = 0.9999 \text{ for dexamethasone acetate}$$

where y is the peak area of analyte and x is the analyte concentration. The results show excellent correlations between peak area and concentration over the desired concentration range.

3.2.3. Accuracy and precision

The accuracy and precision of the method was evaluated by the recovery of known amounts of impurities spiked into stent liquid loading formulation and onto stent surrogates (polymer-coated stainless-steel coupons). The liquid loading formulation, made up with dexamethasone, PC-based polymer [16], butylated hydroxytoluene (BHT), dissolved in a solution of ethanol and 1-butanol, is the formulation used to spray dexamethasone onto stents during manufacture of the drug-eluting stents. Stent surrogates are small PC polymer-coated stainless-steel discs that have similar surface area to that of the stents. Known amounts of dexamethasone acetate, corresponding to 0.025, 0.125 and 0.175 μg ml^{-1}, were added in triplicate into stent loading formulation and onto stent surrogate coupons. The accuracy of the method reported as the percent recovery of dexamethasone acetate, ranged from 89.6 to 105.8%, as shown in Table 2. Additionally, the intermediate precision of the method was assessed by six analyzes of spiked dexamethasone samples using independent working standard preparations. Two analysts on two separate HPLC instruments using different columns on different days performed the determinations. Dexamethasone acetate was spiked into liquid loading formulation at three levels, corresponding to 0.025, 0.125 and 0.175 μg ml^{-1} dexamethasone acetate concentration. The intermediate precision ranged from 1.6 to 4.2% over the three levels, as shown in Table 3. All data indicate that the method is highly accurate and precise for the determination of dexamethasone related substances and no interference was found from either the excipients in the formulation or components of the surrogates.

3.2.4. Limit of quantitation and limit of detection

Solutions of dexamethasone were prepared at the limit of detection (LOD) and limit of quantitation (LOQ) levels, corresponding to 0.03% (0.008 μg ml^{-1}) and 0.1% (0.025 μg ml^{-1}) of the target sample preparation concentration, respectively. LOD and LOQ samples were each injected seven times into the HPLC. For the LOD solution, the mean response of the 7 injections minus 3.3 times the standard deviation is greater than zero. For the LOQ solution, the mean response of the 7 injections minus 10 times the standard deviation is also found to be greater than zero. Thus, the signal-to-noise levels meet the ICH requirements for LOD and LOQ limits.

3.2.5. Dexamethasone degradation study and LC/MS analysis of degradation products

The degradation of dexamethasone was examined in aqueous buffer solutions of various pH values, under heat, light exposure and oxidative conditions. Table 4 shows the stress conditions used for the study. Control samples and placebo were also prepared and analyzed. The major degradation products formed under each condition were identified by LC/MS and LC/MS/MS. A representative chromatogram of a thermally stressed dexamethasone sample is shown in Fig. 3.

Four major degradation impurities were detected for dexamethasone under stressed conditions and their molecular weights were identified using LC/MS analysis. As shown in Fig. 3, dexamethasone eluted at 12.5 min while the four major degradants were observed at 5.9, 10.9, 21.9 and 26.9 min. Fig. 4 shows positive-ion

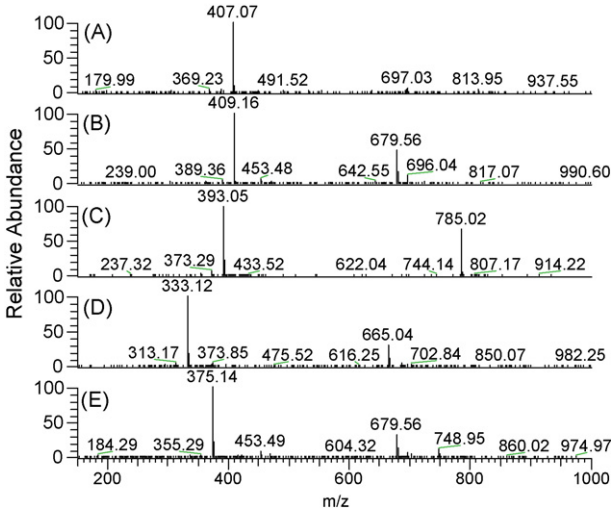

Fig. 4. Positive ESI-MS spectra of (A) dexamethasone-21-oic acid, (B) 6β-hydroxydexamethasone, (C) dexamethasone, (D) 17-oxodexamethasone and (E) 16,17-unsaturated dexamethasone.

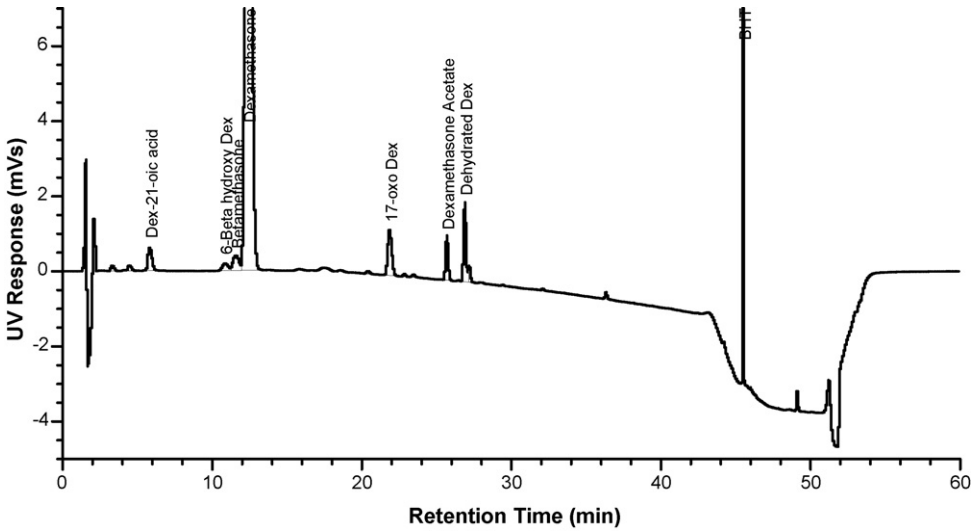

Fig. 5. HPLC chromatogram showing the separation of dexamethasone from major process impurities, degradation products and BHT.

electrospray ionization (ESI) mass spectra for a thermally stressed dexamethasone sample. The LC/MS results of impurities showed peaks of *m*/*z* 407.1, 409.2, 333.1 and 375.1, respectively, presumably corresponding to the protonated molecular ions $(M+H)^+$ of these impurities. The molecular weight of the degradants were determined as 406, 408, 332 and 374 Da. Based on the molecular weights and relevant literature references [12–15], the degradants were proposed to be dexamethasone-21-oic acid (Structure C), 6β-hydroxydexamethasone (Structure D), 17-oxodexamethasone (Structure E) and 16,17-unsaturated dexamethasone (Structure F) with their structures shown in Fig. 2.

Under acidic, basic and thermal stress conditions, the most recognizable product is 17-oxodexamethasone. This type of degradation is observed for hydrocortisone and various other corticosteroids in the literature [17]. 17-Oxodexamethasone is formed by water elimination through an initial enolization of the C_{20}-keto group proposed by Lewbart and Mattox [18]. Other major degradants observed include dexamethasone-21-oic acid and 6β-hydroxydexamethasone, and a minor amount of dehydrated dexamethasone (16,17-unsaturated dexamethasone). Formation of dexamethasone-21-oic acid and 16,17-unsaturated dexamethasone has been reported before for dexamethasone in stress studies [12]. 6β-Hydroxydexamethasone has also been found to be a major metabolite for dexamethasone, typical for a corticosteroid-type of compound [13]. Under an oxidative-stress condition, only 17-oxodexamethasone was observed as the degradation product. For light degradation, the major degradation product is 17-oxodexamethasone with the presence of minor degradation product of 6β-hydroxydexamethasone.

3.2.6. *Specificity and stability-indication*

The specificity of the method was established by demonstrating the separation of dexamethasone process impurities, degradation products, polymer coating material, and BHT from the dexamethasone peak (Fig. 5). Two dexamethasone process impurities, betamethasone and dexamethasone acetate, were spiked and were found to be well separated from dexamethasone. Four major dexamethasone degradation products with structures proposed in Section 3.2.5, presumably dexamethasone-21-oic acid, 6β-hydroxydexamethasone, 17-oxodexamethasone and 16,17-unsaturated dexamethasone, were also well separated from dexamethasone. PC polymer did not interfere with any dexamethasone related substances detection. BHT eluted at about 45.5 min in the HPLC run and did not interfere.

To evaluate whether the method is stability-indicating, the ability of the chromatographic conditions to separate the major degradation products from the manufacturing impurities, excipients and dexamethasone were further examined. Peak purity of the dexamethasone and major degradation peaks in stressed samples was verified using the PDA in the wavelength range of 200–400 nm. It was determined that the dexamethasone peak was spectrally pure and no degradation peaks were detected to co-elute with dexamethasone.

3.2.7. *Evaluation of extraction efficiency*

Ten prototype dexamethasone drug-eluting stents (13 mm in length with 10 μg mm^{-1} target dexamethasone dose) were used for the extraction efficiency study. The stents were first extracted by immersing in 3.0 ml of a mixture of ethanol and pH 3.8 formate

Table 5
Results from the determination of method robustness

Parameter	Value	Dex RT (min)	*R*	*T*	*N*	Standard area R.S.D. (*n* = 6 (%))	Standard RT R.S.D. (*n* = 6 (%))	Standard ratio	Dex acetate (%)
pH	3.6	13.02	15.8	1.2	8,702	0.6	0.2	5.0	0.50
	3.8	12.92	15.7	1.2	8,678	0.2	0.1	5.1	0.50
	4.0	13.25	15.9	1.2	8,673	0.3	0.1	5.1	0.49
Acetonitrile in mobile phase A (%)	25	17.22	21.9	1.1	16,132	0.5	0.0	5.3	0.53
	27	12.96	15.7	1.2	8,662	0.5	0.0	5.0	0.51
	29	9.93	13.2	1.2	8,799	1.2	0.0	5.0	0.51
Column temperature (°C)	43	13.14	15.8	1.2	8,828	1.2	0.0	5.1	0.51
	45	12.96	15.7	1.2	8,662	0.5	0.0	5.0	0.51
	47	12.79	15.6	1.2	8,521	0.9	0.0	5.1	0.51

buffer (50:50, v/v) with sonication and then diluted with 3.0 ml of a mixture of pH 3.8 formate buffer and acetonitrile (70:30, v/v). Forty minutes of sonication was applied per each extraction. After the first extraction each stent was rinsed with a minimal amount of purified water and a second extraction was performed using the same procedure as for the first extraction and 40 min sonication time. No dexamethasone or its related substances were detected for any of the 10 stents in the second extraction. These results suggest that dexamethasone and its related substances are effectively removed with a single extraction.

3.2.8. Robustness

The robustness of the method was examined by small variations of critical parameters, such as buffer pH, composition of mobile phase and column temperature. The pH of formate buffer in mobile phase was varied ±0.2 units, the percentage of acetonitrile in mobile phase was varied ±2% and the column temperature was changed ±2 °C. The system suitability parameters and percent dexamethasone acetate were assessed and data are tabulated in Table 5. Dexamethasone acetate was spiked into dexamethasone solution at about 0.5% level. The results indicate that the method was robust with respect to the key figures of merit. It was observed that the organic composition in mobile phase A is critical for method performance.

3.2.9. Stability

Injections of standards, resolution solution and sample solution were performed after they were stored at room temperature and under refrigerated conditions over time. All solutions are stable for at least 24 h at room temperature. Additionally, sample solutions were found to be stable for 3 days when kept refrigerated, whereas resolution solution and standards were found to be stable for 2 months when kept refrigerated. Solution stability, intermediate precision and applicability of the method in different laboratories all demonstrate the method ruggedness.

4. Conclusions

An HPLC method has been developed and validated for the determination of dexamethasone related substances on drug-eluting stents and in the drug-loading solution. The developed method is accurate, precise and linear across the analytical range. The method is stability-indicating and specific for the determination and quantitation of trace levels of dexamethasone process impurities and degradation products on drug-eluting stent samples. Major dexamethasone degradation products were detected by LC/MS analysis and their possible chemical structures were proposed. This method has especially low limits of detection and quantitation, and was proven to be robust, accurate and precise. The method may be used for rapid analysis of dexamethasone related substances on drug-eluting stent products and applied to other pharmaceutical dosage forms.

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