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Quantitative analysis of sodium dodecyl sulphate by capillary electrophoresis

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Abstract

The surfactant sodium dodecyl sulphate (SDS) is a widely used excipient in solid pharmaceutical formulations. Therefore, it is important to have appropriate analytical methods to measure the SDS content and to confirm its identity in manufactured batches of the preparation. Typically, the analysis is conducted by titrimetry or spectroscopy. However, it would be advantageous to have a more selective method with automation possibilities for the assay. The separation of alkylsulphates by capillary electrophoresis is simple and involves use of indirect detection as they have poor UV absorbance. In this work, a reliable quantitative determination of SDS in a cefuroxime axetil pharmaceutical preparation has been achieved. This is attained primarily by the incorporation of an internal standard. The adsorption of SDS onto filters was also quantified. The level of adsorption was found to vary between filter types and was minimised by filtration of large volumes. It was therefore recommended that large volumes of electrolyte used in micellular electrokinetic capillary chromatography (MEKC) are filtered to ensure repeatable separations. The modified conditions produced a fast, efficient, precise and highly automated means of assaying SDS levels and can provide a useful alternative to established methods of testing.

Keywords: Pharmaceutical analysis; Sodium dodecyl sulphate

1. Introduction

Alkylsulphates or sulphated fatty alcohols consist of the sodium, triethanolamine or other salts of the sulphuric acid esters of the higher fatty alcohols. Sulphated fatty alcohols are widely used in a broad application range by industry such as in the preparation of many "soapless" washing powders and liquids for domestic use. Other household products include the preparation of shampoos, toilet and cosmetic preparations, toothpastes and insecticides. In the pharmaceutical industry sodium dodecyl sulphate (SDS) is the most commonly used alkylsulphate where it is utilised as an excipient in solid formulations. Consequently, it is necessary to have appropriate analytical methods which are capable of confirming the identity and quantitatively measuring the SDS content in manufactured batches of the preparation.

Apart from titrimetry, these substances are routinely determined using fluorimetry [1] or spectroscopy [2]. However it would be advantageous to have a more selective method which can be automated. Capillary electrophoresis (CE) is a relatively new, but highly efficient separation technique which can give good statistically valid reproducible assay methods when care is taken in setting up the method [3].

CE has been used previously to determine SDS in simulated stream water [4] and Nielen [5] studied

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aspects of indirect UV absorbance using the separation of sodium alkyl surfactants as a model system. As the alkylsulphates have very poor UV absorbances they were detected in the CE assay by using indirect UV detection. This method of detection has proven to be a powerful tool in the analysis of ions by CE which includes the analysis of short chain aliphatic carboxylic acids, inorganic anions and metal cations, with different UV absorbing background electrolytes [6–8].

In this work, SDS has been assayed in a developed method which incorporates an internal standard. When the method was established it was proposed not only to use it in the assay of SDS in pharmaceutical preparations but also to look closely at the absorption of SDS on filtering systems which may be used in the assay. SDS is widely used as the micellar agent in micellular electrokinetic capillary chromatography (MEKC). Undissolved particulates in CE buffers can give noisy baselines with irreproducible noise peaks. It is standard practise to filter electrolyte prior to use and if components in the electrolyte such as SDS are adsorbed onto the filter then this presents the possibility for non-repeatability of the method. The effect of any small adsorption losses will be magnified if only a small volume of electrolyte is filtered. The extent of adsorption may also be filter type dependent and therefore it was decided to investigate both the effect of the volume filtered and the type of filter used.

2. Experimental

2.1. Instrumentation

A Beckman P/ACE 5100 instrument (Fullerton, CA, USA) connected to a Hewlett-Packard (Bracknell, UK) HP1000 data system was used. Fused-silica capillaries of 37 cm (30 cm to window)×75 μm I.D. were obtained from Composite Metal Services (Hallow, UK).

2.2. Reagents

Barbital (5,5-diethylbarbituric acid) was obtained from Sigma (Poole, UK) and SDS was obtained from BDH (Poole, UK). Hexane sulphonate sodium salt (internal standard) was obtained from Aldrich (Poole, UK) and the Zinnat tablets were obtained within GlaxoWellcome, Ware, UK.

Table 1
The optimised method conditions

Step	Beckman P/ACE 5100
Capillary dimensions	37 cm (30 cm to detector)×75 μm
Rinse 1	1.0 min (0.1 *M* NaOH)
Rinse 2	1.0 min (buffer)
Injection	1 s
Buffer	8 m*M*±1 m*M* barbital buffer (unadj. pH)
Voltage	10 kV
Temperature	30°C
Detection wavelength	Indirect UV at 214 nm

2.3. Method conditions

The optimised method conditions are given in Table 1.

2.4. Sample preparation

The method development, optimisation and filter study was performed using an aqueous test mixture of SDS and the internal standard (I.S.) at a concentration of 100 μg/ml.

2.4.1. SDS extraction

Three different strength Zinnat tablets were assayed, 125 mg, 250 mg and 500 mg (as cefuroxime axetil) using the method conditions. For each different strength a representative number of tablets were taken and reduced to a powder form using a mortar and pestle. The mass equivalent to one tablet was then transferred to a 50 ml volumetric flask and dissolved in a 100 μg/ml solution of hexane sulphonate (I.S.). Each tablet was analysed in duplicate, having been sonicated for 20 min and filtered prior to analysis.

3. Results and discussion

3.1. Method optimisation

The method used was an adaptation of the procedure by Nielen [5].

3.1.1. Choice of electrolyte ionic strength

The barbital was used as the background absorber and the buffer. The concentration was varied over the range 3–10 m*M*, to establish the effect of buffer concentration on selectivity and sensitivity. The buffer gives a natural pH of ~9.5 and under these conditions the migration order is water (neutral) as the preparation solvent followed by SDS and finally I.S. which is the most mobile anion. Increasing the barbital concentration improved resolution of the components at the expense of increased migration time, as the electroosmotic flow is reduced at higher ionic strengths. However, even with 10 m*M* barbital buffer, acceptable migration times were obtained. It was decided therefore to adopt a buffer concentration of 8 m*M*±1 m*M* as the limits of the method. There was no overall effect on sensitivity at this concentration. Fig. 1 shows a typical separation of the test mixture analysed under the method conditions.

3.1.2. Choice of capillary length, diameter and applied voltage

The initial method development work was performed on uncoated fused-silica capillaries of 37 cm (30 cm length to detector window)×75 μm I.D.. The particular capillary diameter was chosen to allow reasonable method sensitivity with acceptable resolution, and the length to ensure reasonably low currents and acceptable analysis times. However, the voltage should also be optimised in conjunction with the length and bore of capillary. The separation in Fig. 1 was achieved using an applied voltage of +10 kV but lower voltages (<10 kV) produced unacceptably long analysis times, whilst higher voltages decreased the analysis times at the expense of reduced resolution due to increased current and associated heating within the capillary.

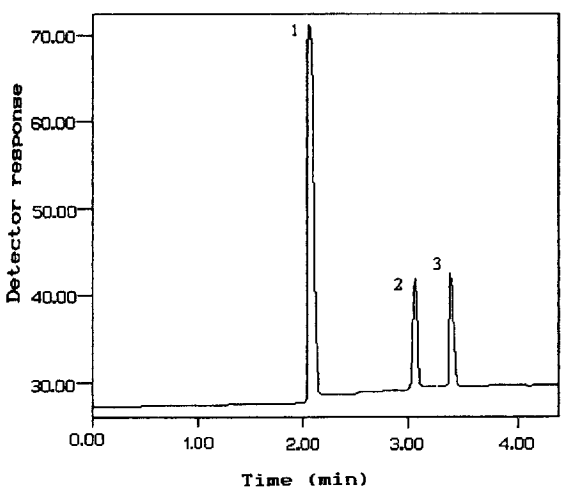

Fig. 1. Separation of SDS test mixture. Separation of the test mixture containing (1) water, (2) SDS and (3) I.S.. Separation conditions: 8 m*M* barbital buffer (unadj.), 37 cm×75 μm capillary, indirect detection at 214 nm, voltage 10 kV and injection 1 s.

3.1.3. Choice of dissolving solvent

Since SDS is readily soluble in water all samples were dissolved in this solvent to maximise peak stacking and resolution. Operation with sample in a low conductivity solvent compared to the separation electrolyte promotes [9] a sampling focusing effect which reduces the initial length of the sample zone within the capillary and increases separation efficiencies and resolution.

3.2. Method performance

Various method validation criteria such as selectivity, precision and linearity of response were assessed.

3.2.1. Selectivity

The migration times of both substances were confirmed by preparing a solution containing SDS and I.S. at 100 μg/ml. This solution was then spiked separately with each of the compounds of interest and analysed by the optimised CE conditions. The results of each separation clearly identifies the migration order and also shows graphically the reproducibility of the migration times.

3.2.2. Precision

Precision of injection was measured by performing ten replicate injections of an aqueous test mixture containing the compounds of interest, at a concentration of 100 μg/ml. The R.S.D. values obtained for the migration times of SDS and I.S. were 0.25% and 0.39% ($n=10$), respectively, which indicates that the optimised conditions gave a stable and repeatable separation. The relative migration time precision for SDS compared to I.S. was 0.10% R.S.D.. The precision for peak areas were 3.79% and 4.10% for

SDS and I.S., respectively. However, an improved R.S.D. of 1.17% was obtained when calculating peak area ratios (against the I.S.), which indicates the importance of employing an internal standard in this analysis.

3.2.3. Sample loading

The injection time was varied from 1 to 10 s to assess the impact of loading on sensitivity. Injections were made in duplicate for each sample loading and mean normalised peak area responses and sampling times were obtained. A linear increase in migration time with increased injection time was observed and a correlation coefficient (R^2) of 0.9894 was obtained. Table 2 shows the injection time (in s) and the corresponding migration time (in min) for the SDS peak. In routine injection sequences consistent injection times should be used to ensure consistent migration times. Increases in peak height with increased sample injection times are not necessarily linear in CE due to increased band broadening at higher loadings. However, there was an approximate six fold increase in peak height moving from a 1 s injection to a 10 s injection time. Therefore, it would be advisable to employ a 10 s injection for trace level determinations.

3.2.4. Detector linearity

Five samples covering the range 1.0–3.2 mg SDS in 25 ml of I.S. solution were injected in duplicate. An acceptable correlation coefficient of 0.9987 was obtained.

3.3. Method application

The previous reported application of this analysis was the monitoring of SDS levels in stream water [5]. In this work the method developed was used to quantitatively determine the levels of SDS in Zinnat tablets.

Table 2
Correlation of migration time (min) with injection time (s) for the SDS peak

Migration time (min)	Injection time (s)
3.12	1
2.99	2
2.94	3
2.87	5
2.56	10

Table 3
The actual and experimentally obtained SDS content for three different strength Zinnat tablets

Strength (as cefuroxime) (mg)	SDS content per tablet (mg)	
	Actual	Obtained
125	2.25	2.18
250	4.5	4.35
500	9.0	8.87

3.3.1. Assay of Zinnat tablets

The SDS content of three different batches of Zinnat tablets (125, 250 and 500 mg) was determined using the optimised method. Table 3 shows the obtained SDS content of each of the different tablet strengths. The results attained are slightly lower than the actual label claim strength and are still well within the typical specification ranges set for excipient contents. This may be due to the fact that SDS is a surface active material and may be retained on the surface of the filters used in the tablet extraction procedure. If SDS is being retained on the surface results would be expected to be slightly lower. Fig. 2 shows a typical chromatogram obtained when analysing a 500 mg tablet under the separation conditions.

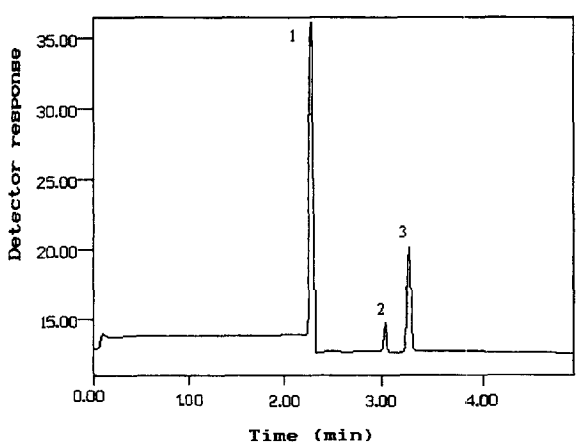

Fig. 2. Separation of the 500 mg Zinnat tablet. Separation of the 500 mg mixture containing (1) water, (2) SDS and (3) I.S. (100 μg/ml). Separation conditions: 8 m*M* barbital buffer (unadj.), 37 cm×75 μm capillary, indirect detection at 214 nm, voltage 10 kV and injection 1 s.

Table 4
The calculated μg/ml concentration of SDS for each of the filter types and volumes used

Filter type	μg/ml		
	0 ml filtered	5 ml filtered	50 ml filtered
Whatman PVDF 0.45 μm	105.3	92.8	97.6
Nylon no-glass pre-inserts	104.9	95.1	99.2
Acro-disk nylon Gelman 0.45 μm	105.1	96.3	103.7
Gelman Glass Acrodisc	105.3	91.3	94.2
Autotop WF plus Whatman	105.2	90.1	93.8

3.3.2. Determination of SDS adsorption onto filters

It may be usual practise to filter sufficient electrolyte (10 ml) to fill the CE vials being used. However, this would result in significant and variable changes in SDS concentration, leading to poor MEKC inter-day repeatability. For example a 15 m*M* SDS concentration after filtration results in a concentration of 12 m*M*, which can significantly affect selectivity in MEKC. It was decided to investigate this hypothesis of SDS adsorption on the surface of a number of commercially available filters using the optimised method conditions. The filters used (see Table 4) were a selection of commonly applied filters in the pharmaceutical industry.

The procedure involved filtering two different volumes (5 ml and 50 ml) of a solution containing SDS and I.S. through each of the filters in duplicate. The resulting solutions were assayed for SDS and the results were compared to a non-filtered solution. Table 4 shows the calculated μg/ml concentration for each of the filter types and volumes used. The results demonstrate that certain filter types are less suitable to filtering solutions with surface active materials and that there is less of an experimental error if larger volumes are filtered.

4. Conclusions

SDS is commonly used in the pharmaceutical industry especially as an excipient in solid pharmaceutical formulations. Therefore it is essential to have appropriate analytical methods to measure the SDS content and also to confirm the identity of manufactured batches. The SDS content of three different batches of Zinnat tablets (125, 250 and 500 mg) was determined using the optimised conditions. The SDS content of each of the different tablets compared favourably to that of the label claim. These optimised conditions were also used to examine the effect of a surface active material (i.e., SDS) on commonly used filters. It was observed that certain filters were less suitable to filtering such solutions and that there was less of an error if larger volumes were filtered. This is a major consideration when operating routine MEKC separations and the filtration of electrolyte should be carefully specified in the method details.

The modified conditions produced a fast, efficient, precise and highly automated means of assaying SDS levels and can provide a useful alternative to established methods of testing.

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