Poster Session 2 – Analytical Chemistry

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Ratio spectra derivative spectrophotometry for the determination of furosemide and spironolactone in a capsule formulation

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The analysis of co-formulated products containing two or more drugs using spectrophotometric methods has been extensively investigated. Techniques such as Vierordt's Method and derivative spectroscopy have found wide application. We have investigated the determination of furosemide and spironolactone in a capsule formulation using these techniques (Vierordt's Method and derivative spectroscopy dA/dλ and $d^2A/d\lambda^2$ applying the zero-crossing technique) following the reported methods of Salem *et al* (1991). In our hands, using standard mixtures, these methods gave unreliable results. We have therefore investigated the use of ratio spectra derivative spectrophotometry for the determination.

The technique of ratio spectra derivative spectrophotometry was developed by Salinas *et al* (1990) and has recently been used for a number of analyses of co-formulated products. The method involves recording of the absorption spectra of mixtures containing both drugs. These spectra are then divided by the absorption spectrum of one of the components at a fixed concentration. This is the ratio spectrum of the component of interest. The first derivative of the ratio spectra is determined and the amplitudes of the derivative signals are plotted against concentration to give a calibration curve. The method is then repeated for the other component. Calibration curves were constructed for furosemide using 2 different strength solutions of spironolactone as the divisor and similarly for spironolactone with furosemide as the divisor. The calibration curves all had r values ⩾ 0.9992. Analysis of test mixtures of furosemide and spironolactone gave mean recoveries (± standard deviations) of 97.13% (± 1.55) and 98.00% (± 2.41). Capsules containing both furosemide and spironolactone were extracted using ethanol as the extraction solvent. Analysis of the capsule contents using the 1 mg/100 mL spironolactone solution as the divisor for furosemide and 0.4 mg/100 mL furosemide solution as the divisor for spironolactone gave recoveries (based on stated content) of 102.13% (± 1.44) for spironolactone and 97.31% (± 0.69) for furosemide. Initial HPLC data for determination of the furosemide content of the capsules indicated a recovery of 95.93% (± 2.76). Thus it appears from this study that ratio spectra derivative spectrophotometry is an appropriate technique for the determination of furosemide and spironolactone in a capsule formulation.

Salem, H., *et al.* (1991) *Spectrosc. Lett.* **24**: 451–470
Salinas, F., *et al.* (1990) *Talanta* **37**: 347–351

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Determination of diclofenac in suppositories: applications in unlicensed and off-label drug use

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The problems associated with unlicensed and off label paediatric drug use have been highlighted in a number of recent papers. Many different examples of such problems have been cited, however, one of the major reasons is the lack of paediatric formulations and subsequent difficulties when adult formulations are adapted for use in children. Conroy & Peden (2001) have investigated the incidence and nature of unlicensed and off label analgesic agents in children. These authors highlighted the problems associated with the lack of paediatric formulations and have described two situations with respect to diclofenac where difficulties might arise. Firstly, when oral administration is required 50 mg (adult)

dispersible tablets may be dissolved in water and an aliquot of the solution used. Secondly, when rectal doses of less than 12.5 mg are required suppositories are cut in half. These authors suggest that both such procedures can potentially lead to medication errors. In the case of suppositories it was suggested that the distribution of diclofenac throughout the suppositories may not be even and also there may be problems cutting suppositories accurately into fractions. A UV spectrophotometric method for the determination of diclofenac in suppositories has been developed and applied to the determination of both whole and fractioned suppositories.

A UV calibration curve for diclofenac in water at 273 nm was constructed for the range 5–50 μg mL^{-1}, typical equation y = 322 × + 0.007 (r = 1). The extraction procedure for the suppositories was based on a modification of the method described by Garcia *et al* (1998). Each suppository was placed in a stoppered conical flask containing water (25 mL) and the suppository dissolved by heating on a water bath at 40–50°C. After 10 min a portion of the contents of the flask (10 mL) was removed and placed in a separate stoppered conical flask. Water (10 mL) was added to the extraction flask to replace the sample removed. This procedure was repeated four times. Combined extracts were made up to volume and the absorbance determined. This procedure was tested on whole suppositories (100 mg:12.5 mg). Ten suppositories of each concentration were randomly selected and assayed, the results indicate the mean was close to 100% of the stated content and the standard deviation was low. Whole suppositories (12.5 mg) were accurately weighed and then cut in half using a scalpel. The two halves were weighed and the estimated content calculated based on the proportional weight relative to the whole suppository (assuming the whole suppository contains 12.5 mg), these suppositories were assayed as above. The results indicate that when the individual halves of the suppositories are assayed for diclofenac content there is no significant difference (*t*-test; *P* = 0.05) between the content in either half.

Conroy, S., Peden, V. (2001) *Paediatr. Anaesth.* **11**: 431–436
Garcia, M. S., *et al.* (1998) *J. Pharm. Biomed.* **17**: 267–273

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Test materials for solution calorimeters

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Solution calorimetry has been used in a number of varying applications, for example, in the areas of quantification of small degrees of amorphous content, identification of polymorphs, and for the investigation of interactions between a drug and a carbohydrate. Therefore, it is essential that a calorimeter should have a test procedure because experimental data must come from validated instruments. Ideally, a test system should be robust, simple to perform, only require materials that are readily available and need no or little preparation prior to use. A few of the suggested calibration reactions are Tris in 0.1 M HCl, NaCl and KCl in water (Archer & Kirklin 2000).

In addition to a range of possible calibration materials, there are a number of different methods available to determine enthalpies of solution from the experimental data provided by the calorimeter. For example, in the case of a solution calorimeter operated under semi-adiabatic conditions, enthalpy of solution may be determined from the temperature offset data using the Regnault–Pfaundler's method, a graphical extrapolation based on the Dickinson method (Wadsö 1966), and a manual integration based method. Thus, the aim of the study was to investigate how each of these methods influence the values for the enthalpy of solution determined for a number of different calibration materials.

Experiments were performed according to the method outlined by Hogan and Buckton (2000) using KCl (samples of 50, 100 and 200 mg), Tris and sucrose as calibrants.

Using all three methods of analysis, the enthalpies of solution for KCl had the lowest standard deviation. For KCl there was a significant difference in enthalpy between the sample masses and also between the methods of analysis (p < 0.05). For all three materials the manual integration method was found to be most consistent when looking at the standard deviation (Table 1) and also produced an

enthalpy value that was the closest to the certified enthalpy of solution from the National Bureau of Standards of 17.584 ± 0.05 kJ/mol.

Table 1 comparing the three methods of analysis, using the results of solution calorimetric experiments with KCl in water (sample sizes of 100 and 200 mg).

Manual ΔH (kJ/mol)	Regnault–Pfaundler's ΔH (kJ/mol)	Dickinson's ΔH (kJ/mol)
17.556 ± 0.019	17.664 ± 0.086	17.316 ± 0.084

For all methods and materials the variance was found to be relatively low, with the largest source of error due to the variance in the magnitude of the loading mass.

Archer D. G., Kirklin D. R. (2000). *Thermochimica Acta* **347**: 21–30
Wadsö I. (1966) *Science Tools* **13**: 33–39
Hogan S. E., Buckton G. (2000) *Int. J. Pharm.* **207**: 57–64