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Short communication

A multicommuted flow system for the determination of dextrose in parenteral and hemodialysis concentrate solutions

Moisés Knochen*, Mariela Pistón, Lourdes Salvarrey, Isabel Dol

Universidad de la República, Facultad de Química, Departamento "Estrella Campos", Cátedra de Análisis Instrumental, Av. Gral. Flores 2124, Casilla de Correo 1157, 11800 Montevideo, Uruguay

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Abstract

A new method is presented for the automation of the determination of dextrose in parenteral and hemodialysis solutions. The method is based on multicommutation flow analysis (MCFA) and exploits enzymatic reactions providing a colored derivative that is detected spectrophotometrically (Trinder's method). The reagent, comprising glucose oxidase, peroxidase, 4-hydroxybenzoate and a buffer was obtained from a commercial kit for the determination of glycemia.

The flow system used three 3-way solenoid valves operating under computer control. The necessary software was developed for the purpose and compiled in QuickBASIC 4.0

The influence of some operating variables (segment size, number of segments and reactor length) was studied.

Calibration curves in the range 0–1 g/L presented a slight curvature and were fitted with a second-degree polynomial ($h = -0.0632C^2 + 0.6039C + 0.166$, $r^2 = 0.9973$, h being the peak-height (absorbance) and C the concentration in g/L).

The method was validated by analyzing artificial samples presenting accurately known concentrations of dextrose, and comparing the results with the known value and with value obtained by polarimetry. Recoveries were in the range 96.6–100.2%, and the difference with the polarimetric analysis was in the range 0.1–3.3%. Precision (R.S.D.,%) was better than 2.4%.

Sampling frequency of the system was 90 samples/h, with a reagent consumption of 0.14 mL per sample.

Keywords: Multicommutation flow analysis; Dextrose; Enzymatic determination; Parenteral solutions; Hemodialysis solutions

1. Introduction

Quality control of the production of contemporary pharmaceutical laboratories involves a large number of analytical determinations comprising many analytes in a number of different matrixes. The growth in the quantity of lots manufactured, and the simultaneous pressure for increased productivity and reduced costs, forces the adoption of automation in the laboratory [1,2].

Besides the obvious advantages of faster analysis and reduced personnel need, automation may convey some fringe benefits such as enhanced precision, reduced reagent consumption and waste generation, and less glassware usage.

Quality control laboratories in the pharmaceutical industry tend to adhere to well-established official methods such as those published in the pharmacopeias, for instance, the United States Pharmacopeia [3]. However, the possibility of automation is not excluded, as long as equivalence of results can be demonstrated through validation.

Among the pharmaceutical products whose control benefits from automation, large-volume parenteral solutions and hemodialysis concentrate solutions have an important place. These products are used in large amounts especially in hospital environments, and many lots are produced daily in the pharmaceutical industry.

* Corresponding author. Tel.: +598 2 9241808; fax: +598 2 9241906.
E-mail address: mknochen@fq.edu.uy (M. Knochen).

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These products consist of aqueous solutions of one or more of several salts such as sodium, potassium, calcium and magnesium chlorides, sodium acetate, sodium lactate, and may contain dextrose and other substances.

The determination of dextrose is usually carried out either by polarimetry, or by a volumetric titration based on its reducing properties. These methods are slow, difficult to automate and their selectivity is questionable. Thus, there exists the need for selective automatic methods for the determination of this analyte.

Among the techniques available for attaining automation with a reduced investment, flow-injection analysis [4,5] has found widespread application in pharmaceutical analysis as reflected in the literature [6–13], reviews [14,15] and a book specifically dedicated to this theme [16].

A different flow technique introduced more recently called multicommutation flow analysis (MCFA) [17–20] shows interesting advantages for automation, and is also being used in the pharmaceutical and related fields [21–25]. Flow-injection analysis is based primarily on the injection of a well-defined volume of sample (and eventually of reagents) in a carrier stream by means of one or more injection valves fitted with sampling loops. On the other hand, MCFA is based on flow systems, where a number of independent commutators (usually solenoid valves) are used to configure a flow network, each commutator being independently actuated under computer control. MCFA allows the implementation of a new sampling technique called binary sampling [17], where a number of segments of sample, reagent and carrier are successively inserted in the analytical path. When compared with FIA, this approach may be more flexible, allowing modifications of the sample and reagent volumes to be carried out easily. Besides, changes in the system and even the implementation of different systems can be carried out under computer control without the need of modifying physically the connections.

Methods exploiting the use of flow-injection analysis for the determination of metals in parenteral and hemodialysis solutions have already been published either for the determination of those formulated as active substances, such as metallic salts [26] as well as of contaminants [27]. However, in a revision we have found no reference to publications pertaining to the application of flow-based methods to the automation of the determination of dextrose in these pharmaceuticals.

In this work, a system based on the concept of multicommutated flow analysis was developed for the selective automated determination of dextrose in parenteral and hemodialysis solutions. In order to attain a high selectivity, it was decided to explore the use of a method exploiting an enzymatic reaction.

The method developed was based on work by Trinder [28]. This enzymatic method for the determination of dextrose is widely used in clinical analysis. A number of commercial kits are available for this determination. The reactions involved in Trinder's method, as applied to the current work are:

$$\text{Glucose} + O_2 + H_2O \xrightarrow{\text{GOD}} \text{Gluconic acid} + H_2O_2$$

$$2H_2O_2 + \text{4-aminoantipyrine} + \text{4-hydroxybenzoate} \xrightarrow{\text{POD}} \text{Quinoneimine}$$

where GOD stands for glucose oxidase and POD for peroxidase.

The quinoneimine formed is a colored substance with maximum absorption at 505 nm, allowing the use of colorimetric detection.

2. Experimental

2.1. Instruments

A Shimadzu (Kyoto, Japan) UV-240 recording spectrophotometer was used as detector. It was fitted with an 80 μL quartz flow cell (Hellma, Müllheim, Germany).

The instrument was set at 505 nm and was operated in the time scan mode. Recordings of the signals were obtained from the graphic recorder–printer of the instrument, which also provided peak-height measurements.

An Alitea (Stockholm, Sweden) C8/2-XV peristaltic pump, fitted with Tygon® tubing was used for pumping the carrier, sample and reagent.

The MCFA system employed NResearch (West Caldwell, NJ, USA) 161T031 3-way 12 V solenoid valves. These valves were controlled using the individual bits of the parallel LPT1 port of the computer via a lab-made DC transistor interface.

Reactors and connections were made from stock Teflon FEP tubing (0.8 mm internal diameter).

A thermostatic bath set at 37 °C was used to keep the reactor's temperature constant throughout the experiments.

Polarimetric measurements were made in a Zuzi 412 automatic polarimeter.

2.2. Computer control

The MCFA system was operated by means of purpose-written software compiled in QuickBASIC 4.0 language and running under MS-DOS 6.0 in a notebook computer.

2.3. MCFA system

The MCFA system (Fig. 1) consisted of a peristaltic pump (P), three 3-way solenoid valves (V1–V3), reactor R1 (in a thermostatic bath) and spectrophotometer used as detector (D).

Valve V1 was used for the introduction of the sample (S), V2 for the reagent (R) and V3 for water, which was used as carrier (C). When not being introduced to the system, sample