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Single interface flow analysis with accuracy assessment

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ABSTRACT

Single interface flow systems (SIFA) present some noteworthy advantages when compared to other flow systems, such as a simpler configuration, a more straightforward operation and control and an undemanding optimisation routine. Moreover, the plain reaction zone establishment, which relies strictly on the mutual inter-dispersion of the adjoining solutions, could be exploited to set up multiple sequential reaction schemes providing supplementary information regarding the species under determination. In this context, strategies for accuracy assessment could be favourably implemented. To this end, the sample could be processed by two *quasi*-independent analytical methods and the final result would be calculated after considering the two different methods. Intrinsically more precise and accurate results would be then gathered.

In order to demonstrate the feasibility of the approach, a SIFA system with spectrophotometric detection was designed for the determination of lansoprazole in pharmaceutical formulations. Two reaction interfaces with two distinct π-acceptors, chloranilic acid (CLA) and 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) were implemented.

Linear working concentration ranges between 2.71×10^{-4} to 8.12×10^{-4} mol L^{-1} and 2.17×10^{-4} to 8.12×10^{-4} mol L^{-1} were obtained for DDQ and CLA methods, respectively. When compared with the results furnished by the reference procedure, the results showed relative deviations lower than 2.7%. Furthermore, the repeatability was good, with r.s.d. lower than 3.8% and 4.7% for DDQ and CLA methods, respectively. Determination rate was about 30 h^{-1}.

1. Introduction

Analytical flow systems with accuracy assessment are valuable resources in routine laboratories as they can provide a reinforced guarantee regarding the quality of the obtained results, as well as additional information on the specificities of a particular set of samples, mainly in terms of matrix effects, assuring a more appropriate management of the routine process control. The concept of accuracy assessment relies on processing the sample simultaneously by two *quasi*-independent analytical methods thus enabling intrinsically more accurate results given that the final analyte concentration is calculated by taking into consideration the results provided by the two methods.

Quality control of pharmaceutical formulations, either during the production stage, as final products or even for screening counterfeit medicine is a crucial concern demanding the selection of accurate, robust and expeditious analytical techniques yielding reliable results.

As emphasised by Oliveira et al. [1], one of the main advantages of automated flow-based analytical methodologies is the high sampling throughput they usually provided, which is mainly supported by the efficient management of all solutions involved, the plain transport of the reaction zone towards detection and the unneed for measurements under equilibrium conditions.

This evident advantage of flow analysis has not been fully exploited in most of the analytical circumstances, even when a bulky sample analysis is required, due to operational limitations not directly related with the determination itself but mainly with sample collecting and pre-treatment steps. However, when this limitation does not exist, as is the case of pharmaceutical formulations analysis, the high sample throughput provided by automated flow-based methodologies could be used to improve results quality.

The application of real time accuracy assessment in a flow analysis was initially proposed in a multi-commutation flow system [1] and subsequently in sequential injection analysis (SIA) [2–6]. While the multi-commutated flow manifold was a relatively complex set up, the SIA technique upheld a more straightforward configuration that allowed the simultaneous implementation of different analytical methods in the same manifold without the need to physically reconfigure it. The recently proposed SIFA systems [7] present some additional advantages in relation to typical flow systems, as they rely on the fact that well-defined and compelling sample and reagent volumes no longer have to be optimised because reaction development depends exclusively on the establishment of a unique reaction interface where mutual sample and reagent interpenetration occur.

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This aspect facilitates system configuration thus enhancing simplicity and operational versatility.

In this work the SIFA concept was further extended by establishing two single reaction interfaces that were applied in the spectrophotometric determination of lansoprazole in pharmaceutical formulations upon simultaneous reaction with the π-acceptors chloranilic acid (CLA) and 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ). The mean of the results obtained by the two spectrophotometric methods provided a more accurate result, showing the viability of a SIFA system with accuracy assessment. Formation of charge transfer complexes between lansoprazole, as electron donor, and π-acceptors CLA and DDQ was for the first time exploited for the spectrophotometric monitoring of this drug in pharmaceutical formulations.

Lansoprazole, 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl] methyl] sulphinylbenzimidazole, is an important proton pump inhibitor being used in the treatment of peptic ulcer disease and in other health conditions where inhibition of gastric secretions may be beneficial, such as dyspepsia, gastro-oesophageal reflux disease and Zollinger–Ellison syndrome [8].

The United States Pharmacopoeia [9] is the only reference that presents the assay of lansoprazole, describing a high performance liquid chromatographic method. Furthermore, several analytical methods relying on electrochemistry [10–12], chromatography [13–26], capillary electrophoresis [27] and spectrophotometry [28–33] have been reported for the determination of lansoprazole in biological fluids and pharmaceuticals. Even though some of them are rather selective, they also have important shortcomings such as utilisation of expensive instrumentation, complex operation and maintenance, low sample throughput as they may require several minutes per assay cycle for sample incubation or may involve lengthy procedures such as those requiring preparation of chromatographic columns or working electrodes. A flow injection (FIA) system has been also reported for the determination of lansoprazole with UV detection [34].

2. Experimental

2.1. Reagents and solutions

Lansoprazole was purchased from Sigma (St. Louis, MO, USA). A 2.71×10^{-3} mol L^{-1} stock solution was daily prepared by dissolving 25 mg in 1.0 mL of a 0.1 mol L^{-1} NaOH solution and diluting up to 25 mL with absolute ethanol (Panreac, Barcelona, Spain). Working standard solutions were prepared by suitable dilutions with absolute ethanol.

Chloranilic acid (CLA, BDH, Poole, UK) and 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ, Sigma, Steinheim, Germany) were used without further purification. The 1.0×10^{-3} mol L^{-1} CLA and DDQ solutions were daily prepared by dissolving 20.9 mg and 22.7 mg of solid, respectively, in 100 mL of absolute ethanol.

2.2. Sample preparation

Commercial capsules with nominal contents of 15 and 30 mg of lansoprazole were analysed. To this end, ten capsules were emptied and the mass of the collected contents was weighted and finely grounded. An accurately weighed powder equivalent to about 15 mg lansoprazole was dissolved in a minimum quantity of a 0.1 mol L^{-1} NaOH solution, diluted with absolute ethanol up to 25 mL, and then filtered through a 0.45 μm membrane filter. Then this solution was conveniently diluted with absolute ethanol to fit the calibration curve.

2.3. Apparatus

The single interface flow system comprised three 10-μL per stroke solenoid micro-pumps (Bio-Chem Valve Inc., Boonton, USA) and a model USB2000 UV–Vis Ocean Optics (Dunedin, USA) fibre optic wavelength scanning spectrophotometer furnished with an acrylic Z-shaped flow cell (inner volume = 10 μL, optical path = 10 mm). The reaction coil was made of 0.8 mm i.d. PTFE tubing. Homemade end-fittings and connectors were also used.

A Pentium-I based computer equipped with a model PCL-711B PC-LABCard (Advantech, Cincinnati, OH) interface card was used for system control and for data acquisition and processing; software was developed in Microsoft Quick-Basic 4.5. A CoolDrive (NResearch Inc., West Caldwell, USA) or ULN2003-based homemade power drives [35] were used to operate the solenoid micro-pumps.

2.4. Flow manifold and procedure

The flow manifold (Fig. 1) comprised three solenoid pumps (P_1, P_2 and P_3) for inserting and propelling the sample and reagent solutions. The repetitive pump on/off switching created a pulsed flowing stream in which the pulse volume corresponded to the pump stroke volume.

The analytical cycle was started by establishing a baseline, which was accomplished with the DDQ π-acceptor solution. To this end, P_1 was actuated for propelling DDQ solution through the reaction coil and the detector. Subsequently, P_2 was actuated, P_1 was switched off and the sample solution (120 pump strokes of 10 μL) was inserted into the analytical path establishing the first single interface. Next, P_3 was actuated, P_2 was switched off and the CLA solution was propelled into the detector establishing the second single interface (Fig. 2). The reaction products formed as a consequence of the mutual sample/π-acceptor intermingle produced analytical signals, which were recorded when the respective reaction interfaces passed through the spectrophotometric flow cell. The absorbance of the lansoprazole–DDQ complex was measured at 462 nm whereas the lansoprazole–CLA complex was monitored at 526 nm.

2.5. Reference method

Aiming at the evaluation of the accuracy of the results obtained with the developed procedure, lansoprazole pharmaceutical formulations were analysed according to the United States Pharmacopoeia [9], by high performance liquid chromatography.

3. Results and discussion

3.1. Chemical parameters

Influence of DDQ and CLA concentrations was investigated between 1.0×10^{-4} and 2.0×10^{-3} mol L^{-1}. In both cases the obtained analytical

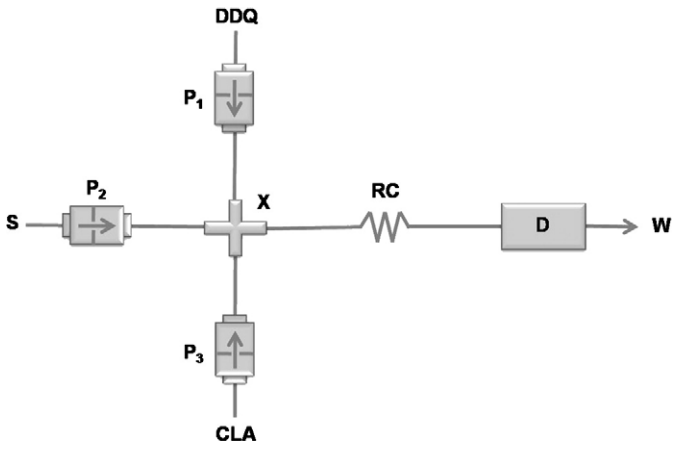

Fig. 1. Single interface flow manifold for the determination of lansoprazole. Legend: P_1, P_2, P_3: solenoid micro-pumps; DDQ: 2,3-dichloro-5,6-dicyano-p-benzoquinone; S: sample; CLA: chloranilic acid; X: confluence; RC: reaction coil; D: spectrophotometric detector; W: waste.