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Automated solid sample dissolution coupled with sugaring-out homogenous liquid-liquid extraction. Application for the analysis of throat lozenge samples

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ABSTRACT

A novel automated procedure for analysis of solid samples based on the on-line dissolution of solid sample and sugaring-out reagent in water-acetonitrile mixture coupled with sugaring-out homogenous liquid-liquid extraction was developed. The procedure was performed in a mixing chamber of a stepwise injection analysis manifold. The performance of the suggested approach was demonstrated by the determination of 2,4-dichlorobenzyl alcohol, amylmetacresol, Yellow Orange S, Azo Rubine and Ponceau 4R in pharmaceutical samples. After phase separation, the upper acetonitrile phase containing 2,4-dichlorobenzyl alcohol, amylmetacresol and lower aqueous phase containing artificial dyes were sequentially analyzed. Under optimal experimental conditions the linear ranges were found to be 0.1–10 mg L^{-1} for 2,4 dichlorobenzyl alcohol, 0.5–50 mg L^{-1} for amylmetacresol, and 1–100 mg L^{-1} for artificial dyes. The sample throughput was 10 h^{-1}. The proposed method was successfully applied for the automated analysis of commercial throat lozenges and the analytical results agreed fairly well with the results obtained by reference HPLC-UV method.

1. Introduction

In recent years, the homogenous liquid-liquid extraction (HLLE) has been investigated as an alternative to the conventional liquid-liquid extraction for the separation and preconcentration of the analytes [1–2]. Several modes of HLLE have been developed such as salting-out HLLE [3], counter current salting-out HLLE [4–6] and sugaring-out HLLE (SHLLE) [7,8] among others. The principles, advantages and shortcomings of HLLE as well as its application for preconcentration of metal and metalloid species hyphenated with various detection systems was discussed [9]. The salting-out HLLE utilizes the salt-induced phase separation phenomenon whereby the organic phase is separated from the homogeneous solution and simultaneously the target analytes are extracted into the separated organic phase when a salting-out reagent is added. In the counter current salting-out HLLE aqueous homogeneous solution of the analytes containing disperser and extraction solvents is transferred into a narrow bore tube which is filled partially with salting-out reagent. During passing the solution through the tube, fine droplets of the organic phase are produced at the interface of solution and salt which go up through the tube and form a separated layer on the aqueous phase. The use of polar solvents in salting-out HLLE results in high extraction efficiency. Besides that simplicity of operation, rapidity, low sample volume, low cost and relatively high enrichment factors can be mentioned as its advantages. However, the use of a high concentration of salts (e.g., K_2HPO_4) for phase separation may lead to alter the pH of the sample and may react with the analyte(s) and sample matrixes [10]. The sugaring-out reagents (monosaccharide or disaccharide) allow excluding the negative effect of the inorganic salts used in salting-out HLLE [11]. The SHLLE assumes the separation of the organic phase by the addition of a sugaring-out reagent and extraction of the analyte into water-soluble organic solvent. The SHLLE has been successfully applied to separate and preconcentrate various analytes [12–14] from different samples.

It should be noted that all described SHLLE techniques were implemented only for analysis of aqueous sample solutions. To the best of our knowledge, the SHLLE for the analysis of solid phase samples has not been reported in any literature. Another important and rapidly growing trend existing in modern analytical chemistry is automation of analytical procedures. Flow based methods can be recognized as a universal tool for automation of a wide variety of analytical procedures including various liquid-liquid extraction methods [15–25]. However, the automation of SHLLE has not been reported yet.

Therefore, the aim of this study was to develop the automated sample preparation procedure for the analysis of solid samples based on its dissolution coupled with sugaring-out homogenous liquid-liquid

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extraction (D-SHLLE). To demonstrate the efficiency of the suggested approach, the proposed procedure was applied for the determination of 2,4-dichlorobenzyl alcohol, amylmetacresol, Yellow Orange S, Azo Rubine and Ponceau 4R (ESI Fig. 1) in throat lozenge samples using a stepwise injection analysis (SWIA) [26–29] manifold that includes a mixing chamber (MC) connected to the atmosphere and this feature was used for the implementation of the effective mixing and phase separation.

2. Experimental

2.1. Reagents and solutions

All chemicals and reagents used were of analytical grade. Yellow Orange S, Azo Rubine, Ponceau 4R, 2,4-dichlorobenzyl alcohol, amylmetacresol, glucose, fructose and sucrose were supplied from Sigma-Aldrich. Ultrapure water was purified by means of a Millipore™ water purification system and was used throughout the work.

The stock solutions of dyes (0.5 g L^{-1}) were prepared in water and stored in a fridge. The working solutions of dyes were prepared by dilution of the stock solutions with water. The stock solutions of 2,4-dichlorobenzyl alcohol and amylmetacresol (0.5 g L^{-1}) were prepared in acetonitrile and stored in a fridge in the dark bottles. Methanol (Sigma-Aldrich) and 40 mM ammonium acetate aqueous solution (pH = 5) were used as eluents in HPLC-UV analysis.

2.2. Samples and sample preparation

The commercially available lozenges (brand A, brand B, brand C) were used for the analysis. The samples were mechanically crushed in a mortar and immediately analyzed.

2.3. Manifold and apparatus

The SWIA manifold (Fig. 1) consists of eight-way valve, peristaltic pump with flow rate ranging from 0.5 to 5 mL min^{-1}, 5 mL syringe pump (FIAlab ® Instrument Systems Inc., Bellevue, USA), the mixing chamber (a cylindrical-shaped polypropylene tube, 20 mm height and 10 mm i.d.) with PTFE filter prepared according to [30], pressed into a funnel-shaped bottom and communication tubes (PTFE, 1.02 mm i.d.). The manifold was equipped with USB 4000 spectrometer (Ocean Optics Inc., USA) with a 10 mm path-length flow cell (FIAlab® Instrument Systems Inc., Bellevue, USA), optical fibers QP400–2–UV–VIS (Ocean Optics Inc., USA) and Model D 1000 CE UV source (Ocean Optics Inc., USA). The analyzer was operated automatically using a computer.

HPLC-UV system LC-20 Prominence (Shimadzu, Japan) was used for reference measurement.

2.4. The SWIA procedure

At the first stage, 10 mg of the sample powder and 75 mg of glucose were placed on the PTFE filter of the MC (Fig. 1). Then 0.35 mL of water-acetonitrile mixture (1:1.5, v:v) (port 1) was aspirated through the valve (1) into a holding coil by the syringe pump and then transferred into the MC.

After completion of this operation, the syringe pump was switched on airport and 5 mL of air was aspirated into the syringe pump. Then air was transferred (rate 5 mL min^{-1}) by forward movement of the syringe pump through the port 8 into the MC and the sample and glucose were dissolved and the formation of the upper acetonitrile and lower aqueous phase was observed.

Then pause was keep (20 s) to complete the phase separation and lower aqueous phase containing a dyes was delivered by movement of the peristaltic pump through the flow cell of UV–Vis detector to the waste. The absorbance was measured under stop-flow conditions for 10 s. The wavelength was chosen depending on the dye type of throat lozenge sample (484, 510 or 520 nm for Yellow Orange S, Azo Rubine and Ponceau 4R, respectively).

Then 0.15 mL of water-acetonitrile mixture (1:1.5, v:v) (port 1) was aspirated through the valve (1) into the holding coil by the syringe pump and delivered into the MC to dilute the acetonitrile phase containing of 2,4-dichlorobenzyl alcohol and amylmetacresol. After that the solution was moved from the MC into the flow cell of UV–Vis detector by movement of the peristaltic pump. The absorbance values for 2,4-dichlorobenzyl alcohol and amylmetacresol were simultaneously measured under stop-flow conditions (220 and 280 nm for 2,4-dichlorobenzyl alcohol and amylmetacresol, respectively) for 10 s and solution was discharged to waste.

At the final step, all the components of the manifold were washed with water-acetonitrile mixture. The measurement of the analytical signal for a blank solution was carried out using the above-mentioned algorithm, but in this case without adding of sample.

2.5. The HPLC-UV procedure

The results of the SWIA determination of 2,4-dichlorobenzyl alcohol, amylmetacresol and dyes were compared with those obtained by means of HPLC (column Luna C18 (150 × 4 mm, 5 μm particles size)) [31] using UV detection at 250 nm. A 1 g of sample was ground and dissolved in 10 mL of water-methanol mixture (1:1, v:v). The mobile phase used was 40 mM ammonium acetate aqueous solution (pH = 5) and

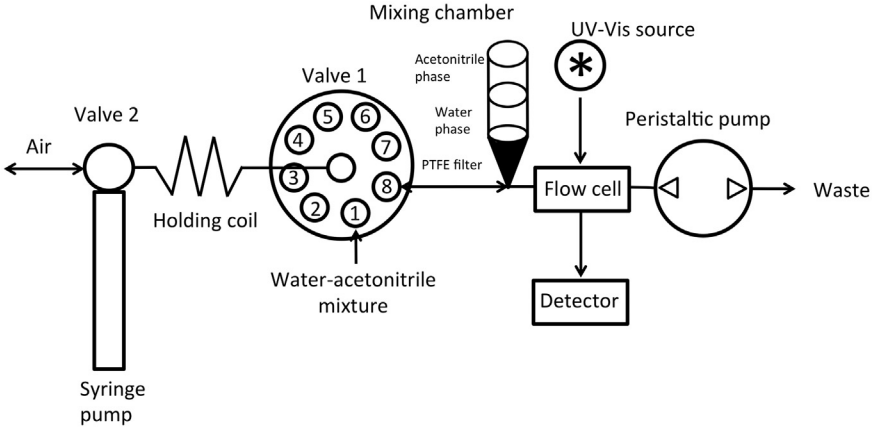

Fig. 1. The manifold for automated D-SHLLE system for the analysis of throat lozenge samples.