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Review

# Single-drop microextraction as a powerful pretreatment tool for capillary electrophoresis: A review

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## HIGHLIGHTS

- SDME is a convenient and powerful preconcentration and sample cleanup method for CE.
- SDME-CE has been applied to the analysis of target analytes in complex matrices.
- SDME-CE has been hyphenated with other on-line preconcentration techniques in CE.

## GRAPHICAL ABSTRACT

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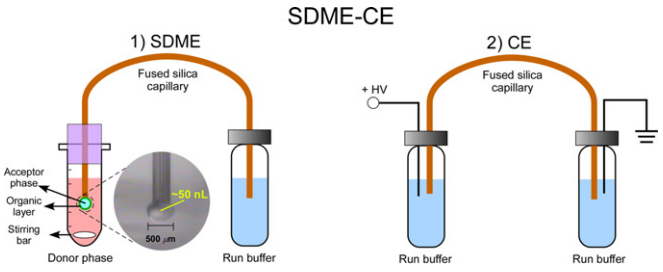


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## ABSTRACT

Single drop microextraction (SDME) is a convenient and powerful preconcentration and sample cleanup method for capillary electrophoresis (CE). In SDME, analytes are typically extracted from a sample donor solution into an acceptor drop hanging at the inlet tip of a capillary. The enriched drop is then introduced to the capillary for CE analysis. Since the volume of the acceptor drop can be as small as a few nanoliters, the consumption of solvents can be minimized and the preconcentration effect is enhanced. In addition, by covering the acceptor phase with an organic layer or by using an organic acceptor phase, inorganic ions such as salts in the sample solution can be blocked from entering the acceptor phase, providing desalting effects. Here, we describe the basic principles and instrumentation for SDME and its coupling with CE. We also review recent developments and applications of SDME-CE.



**Contents**



*Abbreviations:* BGE, background electrolyte; C$^4$D, capacitively-coupled contactless conductivity detection; EOF, electroosmotic flow; LIF, laser-induced fluorescence; LLE, liquid–liquid extraction; LPME, liquid phase microextraction; LVSS, large volume sample stacking; LVSEP, large volume stacking using an electroosmotic flow pump; SDME, single drop microextraction; SPE, solid phase extraction; SPME, solid phase microextraction.

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## 1. Introduction

High efficiencies and rapid separations in capillary electrophoresis (CE) are obtained when a narrow-bore (typically 25–100 μm) capillary is used as originally described by Jorgenson and Lukacs [1–4]. However, the use of a narrow-bore capillary results in a major limitation in detection sensitivity, especially for – the most commonly used – UV/Vis absorbance detection. Due to the small optical pathlength of the capillary, limits of detection (LODs) are inferior to those obtained with a conventional HPLC detection cell (1 cm width). Moreover, the injected sample volume in CE is usually limited to 1–2% of the total capillary volume (typically >0.1 μL). Otherwise, band broadening due to overloading is unavoidable [5].

Several approaches can be undertaken to increase the detection sensitivity in CE. Some of these strategies depend on increasing the optical pathlength of the detection cell through the formation of Z-cells or bubble cells inside the capillary, but these approaches usually impair the resolution due to non-uniform capillary geometry and possible changes in the electric field distribution [6]. Other approaches depend on the use of alternative highly sensitive detection schemes such as laser induced fluorescence (LIF) and mass spectrometry (MS). The major disadvantage of fluorescence detection is that most compounds do not possess native fluorescence; derivatization is therefore required, however it can be a laborious, time consuming, and non-quantitative process. MS is also a very sensitive and selective detector, but its use for sensitivity enhancement in CE has not been fully explored because of the complicated interfaces and special background electrolyte (BGE) compositions needed for CE-MS hyphenation. Furthermore, LIF and MS detectors are relatively expensive to purchase and maintain.

In order to overcome the limitation in detection sensitivity of CE, a number of preconcentration approaches can be used. These approaches can be utilized before, during, or after sample loading into the capillary. Generally, if the preconcentration and CE separation steps are performed separately, the preconcentration approach is referred to as off-line preconcentration. More specifically, the transfer of analytes from the preconcentration to the subsequent separation step is carried out manually in off-line approaches. If the transfer is facilitated via a robotic interface, then the approach is referred to as at-line coupling [7]. In off-line and at-line approaches there is no direct stream of analytes between the two steps of preconcentration and electrophoresis [8]. It is important to mention that off-line and at-line enrichments are facilitated mostly via chromatographic or extractive preconcentration [9]. Understandably, the off-line preconcentration methods are usually laborious and time consuming. Moreover, incomplete transfer of the sample from the preconcentration device to the subsequent CE step may take place; a result from the low solubility of the analytes (as in liquid–liquid extraction, LLE), irreversible adsorption of analytes into the solid phase (as in solid phase extraction, SPE), or loss of analytes during handling. In addition, typical sample