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Review

# New developments in microextraction techniques in bioanalysis. A review

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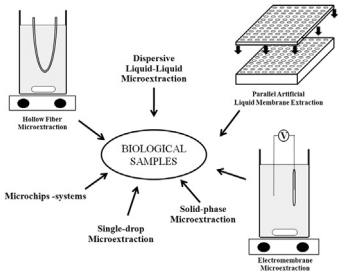
## HIGHLIGHTS

- Recent microextraction methods for bioanalysis are reviewed.
- Fundamentals, recent developments and applications for each method are discussed.
- Trends to miniaturization and on-chip extraction are highlighted.

## GRAPHICAL ABSTRACT

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## ABSTRACT

In recent years, the interest in new extraction methods with lower sample volume requirements, simpler equipment and handling, and lower reagent consumption, has led to the development of a series of microextraction methods based on extraction phases in the microliter order. Nowadays, many references can be found for several of these methods, which imply a wide range of applications referred to both the analyte and the sample nature. In this paper, recent developments in both well-established microextraction techniques (solid phase microextraction, hollow-fiber liquid phase microextraction, dispersive liquid–liquid microextraction, etc.) and recently appeared microextraction procedures (nanoextraction systems, microchip devices, etc.) for the clinical analysis of biological samples will be reviewed and discussed.



**Contents**



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**Abbreviations**

| | |
|---|---|
| AgNPs | silver nanoparticles |
| CE | capillary electrophoresis |
| DART | direct analysis in real time |
| DLLME | dispersive liquid–liquid microextraction |
| EME | electromembrane microextraction |
| FL | fluorescence |
| GC-FID | gas chromatography-flame ionization detection |
| GC-MS | gas chromatography-mass spectrometry |
| GC-ECD | gas chromatography-electro capture detector |
| GF-AAS | graphite furnace-atomic absorption spectrometry |
| HF-LPME | hollow fiber liquid phase microextraction |
| HPLC-CAD | high performance liquid chromatography-charged aerosol detection |
| HPLC-MS | high performance liquid chromatography-mass spectrometry |
| HPLC-UV | high performance liquid chromatography-ultra violet |
| IDLLME | inverted dispersive liquid–liquid microextraction |
| IL-DLLME | ionic liquid dispersive liquid–liquid microextraction |
| ISFME | in-situ solvent formation microextraction |
| LE | liquid extraction |
| LPME | liquid phase microextraction |
| MALDI-TOF MS | matrix-assisted laser desorption/ionization-time of flight mass spectrometry |
| MECK | micellar electrokinetic chromatography |
| MEPS | microextraction by packed sorbent |
| MIPS | molecularly-imprinted polymer synthesis |
| MWCNTs | multi-walled carbon nanotubes |
| PALME | parallel artificial liquid membrane extraction |
| SA-DLLME | surfactant-assisted dispersive liquid–liquid microextraction |
| SDME | single drop microextraction |
| SFODME | solidified floating organic drop microextraction |
| SLM | supported liquid membrane |
| SPE | solid phase extraction |
| SPME | solid phase microextraction |
| SUPRAS | supramolecular solvent-based |
| SWCNTs | single-walled carbon nanotubes |
| TFME | thin-film microextraction |
| USAEME | ultrasound-assisted emulsification microextraction |



## 1. Introduction

Many important fields concerning human health, as medical diagnostics and treatment, medical research, pharmaceutical research and biochemical research, rely on the analysis of one or several chemical or biochemical substances present in living organisms or biological fluids. The analysis of chemical and biochemical substances usually involves identification or structural elucidation, followed by quantification to measure the actual concentration level within the samples. These substances of interest include drugs, drug metabolites, lipids, peptides, proteins, DNA and carbohydrates, among others.

The analysis of chemical and biochemical substances in living organisms and biological fluids is a complicated process, which includes a sample preparation step before its chemical analysis. This step is usually required because (1) most biological samples are incompatible with the analytical instruments, (2) these samples are too complex for direct analysis, as other substances in the sample may interfere during the measurement, and (3) the analytes are typically present at low concentration levels, being not detectable by the analytical instrumentation.

Most commonly used sample preparation procedures generally involve liquid extraction (LE) or solid-phase extraction (SPE). LE is easy to perform, requiring no complicated instrumentation, but with several drawbacks: LE procedures use relatively high amounts of hazardous organic solvents (which represents a serious environmental problem), they can not be easily coupled to the analytical instruments, and their selectivity is limited, leading to the extraction of many matrix components from the sample, which may result in serious interferences in the analytical determination. Finally, taking into account the actual trends to miniaturization of analytical instruments, where the volumes of extracts are in the pico-liter to the micro-liter range, LE (with volumes of extracts in the milliliter or higher range) does not seem to be the best sample-