BAGHDAD JOURNAL OF BIOCHEMISTRY AND APPLIED BIOLOGICAL SCIENCES
2023, VOL. 4, NO. 4, 204-217, e-ISSN: 2706-9915, p-ISSN: 2706-9907
https://doi.org/10.47419/bjbabs.v4i04.226

NARRATIVE REVIEW

Current Development in Bioanalytical Sample Preparation Techniques

Sakshi R. Sangale, Pravin R. Dighe and Manoj R. Kumbhare

Department of Pharmaceutical ChemistryS.M.B.T College of Pharmacy, Dhamangaon, Nashik, Maharashtra, India

ABSTRACT

The preparation of the sample is the most important stage in bioanalysis. Proteins, salts, and other organic compounds with chemical characteristics similar to the target analytes are commonly found in biological samples. As a result, sample preparation is an essential step that improves matrix suitability for analysis in multiple ways, including by separating the analytes and clearing the matrix of obstructive elements. Innovative sample preparation techniques have been more and more popular over the last 10 years due to their advantages over conventional techniques in terms of accuracy, automation, simplicity of sample preparation, storage, and delivery. This article's goal is to raise awareness of the most recent advancements in the processing of bioanalytical samples. Different extraction stages are provided by modern techniques, such as sorbent-based microextraction, and the advantages of bioanalytical approaches have been highlighted.

Keywords: Bioanalysis, Samplepreparation, Sorbentbased microextraction, Biological samples

Received 08-05-2023
Revised 31-10-2023
Accepted 01-11-2023

Corresponding Author
Sakshi R. Sangale
sakshisangale29@gmail.com

DOI https://doi.org/10.47419/bjbabs.v4i04.226

Pages: 204-217

INTRODUCTION

The word"bioanalysis" is used to describe the research and measurement of analytes (such as medicines and metabolites) in natural samples (biofluids or tissues). Bioanalysis is at present included in many examination regions, like the improvement of new medications, scientific investigation, distinguishing proof of biomarkers and doping control. The drug industry has a strong tradition of using bioanalysis to aid with drug disclosure and medication improvement. It also plays a crucial role in toxicokinetic, pharmacokinetic, and pharmacodynamic investigations.

Sample preparation, analyte separation, and detection are the three key elements of a bioanalytical approach. Preparation of sample is pointed toward moving a complex matrix

to a reasonable structure before infusion into the instrument. The value of a sample preparation method: (i) eliminate meddling mixtures, (ii) dispose of particle concealment, and (iii) pre-concentrate the analytes to work on the strategy's responsiveness.[1,2]

Bioanalytical research makes use of a variety of biological s, including blood, serum, plasma, urine, human breast milk, hair, saliva, sweat, and tissue. Likewise, every matrix has one of a kind difficulties. For instance, phospholipids are more prevalent in plasma, while a significant amount of salts are present in urine.[3] Biofluids are frequently used in bioanalysis, including plasma, serum, blood, urine, perspiration, saliva, and tissue. As of late, human breast milk, hair and feces have likewise utilized as biological specimen.[4] A remarkable indicator of drugs and contaminants from the environment is human breast milk.[5]

SAMPLE PREPARATION TECHNIQUES

It is evident that effective and environmentally responsible sample preparation techniques are currently needed. Solvent extraction methods, inclusive LLE, liquid-phase microextraction (LPME), and related optimal approaches for bioanalysis include solid-liquid extraction (SLE). These methods reduce theprice of medication research and increase interest in the pharmaceutical industry.[6] Current research has aimed on the advancement of sample preparation procedures in order to gain advantages. Robotics-based strategies for preparing samples such as SPE, LPME, and LLE have been cybernated, resulting in new and elegant perspectives on bioanalysis.[7]

Solid-phase microextraction (SPME) is a technology that Arthur and Pawliszyn introduced in 1990.[8] Sample collection, preconcentration, and extraction are all done in one step as an example of non-restrictive process that SPME illustrates.[9] This method's benefits include quick and easy operation and excellent precision, improved sample purification, and reduced solvent consumption. SPME simultaneously pre-concentrates and separates volatile and non-volatile samples. Recently, the application of fluorescence-based SPME technology and handheld fluorometers has also provided opportunities for in-situ drug testing.[10,11]

MICROEXTRACTION TECHNIQUES

The goal of the microextraction technique is to use the least quantity of solvent possible. The microextraction technique is tough, versatile, solvent-free and inexpensive.

Advantages: i) Cheap, ii) Easy to use, iii) Little use of Solvent.

Disadvantages: i) Impermanence of drops, ii) Low sensitivity and precision, iii) Limited Solvent choice.

The main micro-extraction techniques developed are:

Single drop microextraction (SDME)

SDME is a practical and affordable little instrument for separating multiple analytes of interest from complex matrices. SDME was introduce by Liu and Dasgupta to address the issue of solvent evaporation.[12] The analyte is divided between the aqueous sample and the microscopicamounts of organic solvent in SDME. Thesingledrop of SDME is theextraction medium. Microdrops are usually composed of organic solvents (e.g. 1-10 uL).[13] There is no carry-over in a straightforward, affordable, and environmentally friendly microextraction method. Small solvent volume usage makes SDME an environmentally favourable analytical procedure that generates little to no waste. Although, the instability and volatility in drop volume are the main drawbacks. In general, direct immersion (DI-SDME) and headspace mode (HS-SDME) are the two key principles that has application to execute SDME.[14]

Stir bar sorptive microextraction (SBSME)

In SBSME, desorption and extraction are essential procedures. A stir bar covered with polydimethylsiloxane is immersed in the sample solution during the analysis.[15] Commercial SBSME requires slightly more than 125 uL of sorbent, which is more than SPME. SBSME cannot be utilised to analyse very hydrophilic substances. To overcome this issue, researchers have proposed the use of molecularly imprinted polymers (MIPs), better coating materials, dual-phase stir bars, and monolithic materials. Carbon Nanotubes, Graphene, Metal-Organic Frameworks (MOFs), Graphene Oxide, Porous Organic Polymers and Monoliths are recently developed materials that are useful for SBSME coating.[16]

Hollow fiber liquid-phase microextraction (HF-LPME)

A little amount of extraction solvent (about 10–20 uL) is placed into a hollow tube made of porous hydrophobic fibre material. A supported liquid membrane (SLM) is produced when an organic solvent that is immiscible with the fibre is added. The solvent becomes immobilised in the pores of the fibre. An affordable and efficient microextraction technique is HF-LPME, which is very simple to programme. Due to the interchangeable fibres, it has greater solvent stability compared to SDME and lacks memory and carry-over effects. Rapidity, high repeatability, clear extract, and a favourable enrichment factor are further benefits. Despite being widely used at the moment, this method has two drawbacks: air bubble production on the fibre surface, which reduces the transfer rate and limits repeatability, and non-polar substance adsorption on the fibre surface, which causes obstruction (for example, in blood, plasma, and urine samples).[17]

Dispersive liquid-liquid microextraction (DLLME)

Dispersiveliquid-liquid microextraction(DLLME) andits variants, suchas sugaring-out assistedliquid-liquidextraction(SULLE), ionicliquid-basedDLLME, deepeutecticsolvent-based DLLME, andultrasound-assisted DLLME(UA-DLLME), allhaveuniqueadvantages. These benefits include the potential for combination extraction, lowest cost, ease of usage, and a high initial concentration factor for the target analytes.[18,19,20] By increasing the exposuresurface between the sampleand the extractant in DLLME, the dispersion approach dramatically improves the kinetics of extraction. Centrifugation used to separate the resultant

emulsion, and the extractant is extracted. [21]

Theuse of DLLME with highlypolar metabolites has beensupportedby numerous investigations (e.g., folate derivatives and neurotransmitters). Pyrethroid insecticides and hexachlorocyclohexane isomers have been detected in milk using DLLME. [22]

Recent advancements in DLLME include, air-assisted DLLME, binary solvent (BS)-DLLME and vortex-assisted DLLME, which solidify floating organic droplets (DLLME-SFO) in an effort to limit the consumption of hazardous solvents in extraction. [23] The simultaneous detection of linezolid, piperacillin, ciprofloxacin, and metronidazole in human plasma samples is another application of DLLME. Tramadol concentrations in urine samples have been measured using BS-DLLME. [24,25]

Electromembrane extraction (EME)

The extraction speed in HF-LPME is influenced by a number of variables, including the partition coefficient between the sample (donor solution) and the organic solvent, the partition coefficient between the acceptor solution and the organic solvent, the volume of the acceptor solution and the sample, the area of the liquid membrane, and the thickness of the stagnant boundary layer between the sample and SLM. [26] The process is still comparatively slow even when these parameters are optimised. The electromembrane extraction (EME) proposal from 2006 addressed this by generating an electrical field across the SLM to move charged materials from the sample through the SLM and into the acceptor solution. [27]

Employing an electrical potential to encourage movement through an extremely thin organic liquid membrane is what makes EME unique. In contrast to the more conventional liquid-liquid extractions made possible by electrical fields, EME has recently gained a lot of interest. This is because this kind of electro-driven device is highly effective when it is in the shape of a thin membrane. EME has also demonstrated excellent potential for real-world bioanalysis applications. [28,29] Recently, antipsychotic medications such risperidone, and haloperidol and aristolochic acid were isolated in total urine and blood were examined by EME-LC-MS/MS. [30,31]

MICROSAMPLE PREPARATION TECHNIQUES

Small sample quantities (<50 uL) of biological fluids are prepared using microsam- ple preparation procedures. They can enhance animal welfare because fewer animals are needed in investigations because the quantity of biological matrices is reduced. [32]

Advantages: i. Allow to construct better Pharmacokinetic/Pharmacodynamic profile and comparison of multiple formulations using the same animalanimal, ii. Less painful and stressful often have fewer requirements on handling and storage.

Disadvantages: Thetechnique often suffers from variations in sample quantification and analysis due to technical errors and biological fluctuations, such as hematocrit.

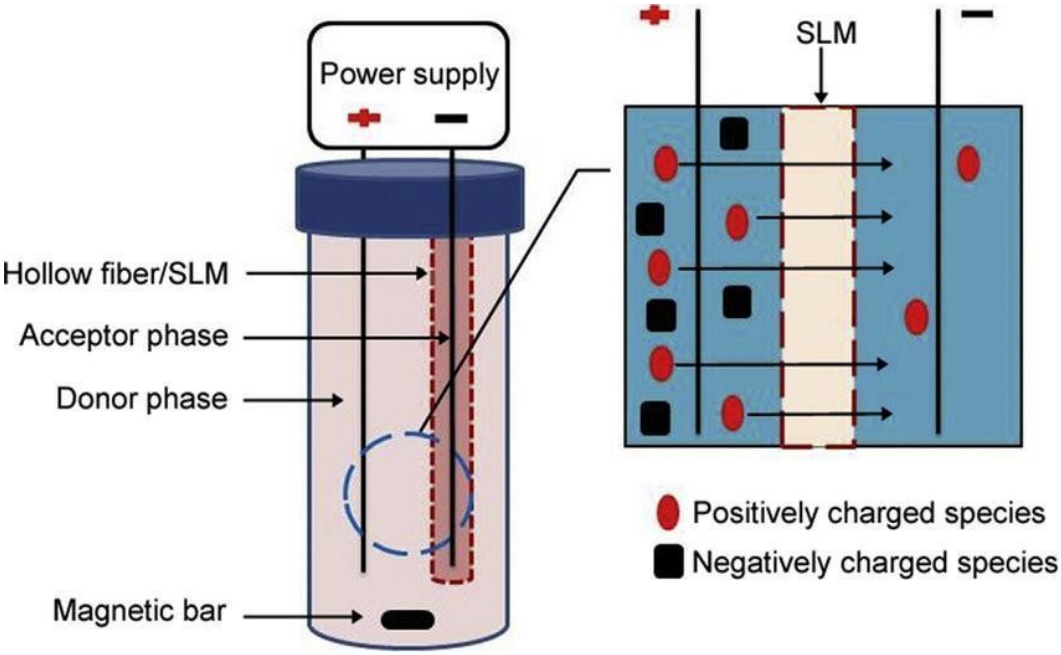

Figure 1 A schematic mechanism of electromembrane extraction.

Cloud point extraction (CPE)

Surfactant solutions that divide in two isotropic phases after becoming hazy are the foundation of CPE. Over LLE, SPME, SPE and CPE has a number of advantages. Fewer samples were required for the analysis because CPE not requires the use of organic solvents. In CPE safe and affordable surfactants are use which have been utilize to measure metals and a variety of chemical moieties (such as medicines, vitamins, and insecticides) in various biological matrices using green surfactant. [33, 34] In bioanalytics, CPE is the preferred technique for saliva analysis. [35] CPE is superior to other sample preparation methods in that it is straightforward, inexpensive, has higher extraction kinetics, and has a favourable environmental profile. Regarding the role of CPE in bioanalysis, there is, unfortunately, little information currently available. A surfactant, such as Triton X-114, was used to quantify the presence of antazoline in human plasma, and this was followed by LC-ESI-MS/MS (liquid chromatography-electrospray ionization-tandem mass spectrometry). [36]

Microdialysis

Microdialysis has been utilised to gather samples devoid of macromolecules inside intricate biological matrices. To acquire a sample through perfusion, a tiny microdialyser is fastened using a membrane that is perm-selective inside the human body. The pharmacokinetic (PK) analysis of a variety of analytes derived from organs including the muscle, brain, blood vessels, liver, tumour, kidney, gastrointestinal tract, and skin has shown that microdialysis is a dominating technique for detecting xenobiotic containing metabolites inthe interstitial space[37 38 39] .

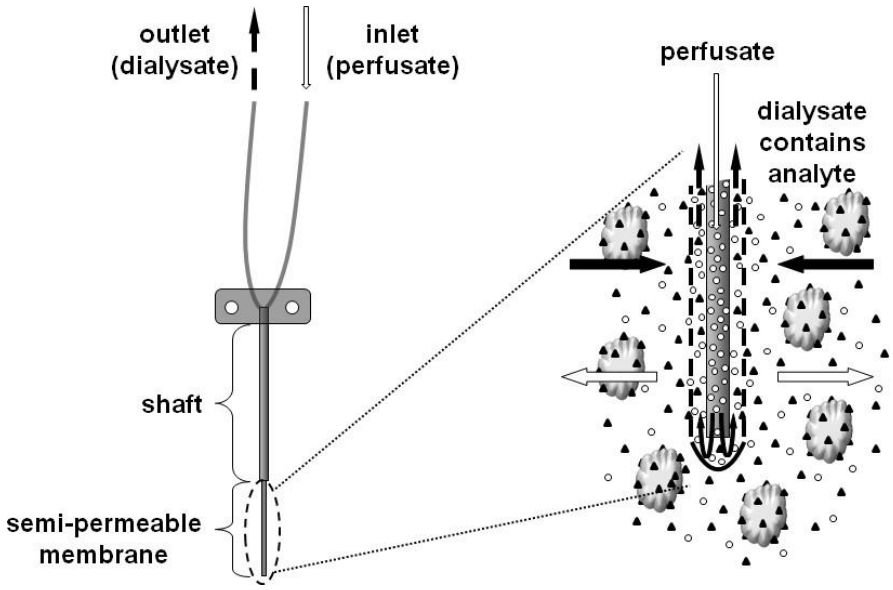

Figure 2 Schematic illustration of microdialysisprobe.

Dried blood spots (DBS)

DBS is based on the idea that biological elements adhere to the surface of a membrane carrier, then dry.[40] DBS has recently attracted a lot of interest in clinical and bioanalytical laboratories. Dried blood spots functions as a key technique for researching novel biomarkers and aiding therapeutic medication monitoring, similar to metabolomics analysis.[41, 42]

Dried plasma spots (DPS)

A recently developed method for the early identification of neurodegenerative disorders, DPS is similar to DBS. The driedplasma spots is aspecialremotebloodcollection devicethat uses two filter papers.[43] Compared to standard plasma collecting methods, it offers a most of advantages. The least amount of biohazard risk can be represented by dried spot collection on filter paper due to its portability, simplicity, and lack of refrigeration. Compared to the traditional techniques of sample preparation, these advantages give DPSs a great deal of flexibility. Trimethoprim, ritonavir, sulfamethoxazole, and fosfomycin have all been found in biological matrices using DPS.[44, 45, 46]

Dried saliva spot (DSS)

Examining the distribution of salivary proteins in the oral cavity with DSS is a low-risk procedure. DSS provides a number of benefits, including affordability and simple, non-

invasive sample collection. [47] In comparison to other approaches, for extraction and sample preparation operations DSS is advantageous and feasible. DSS expands the use of saliva to identify circulating biomarkers, identify matrix metalloproteinase-1 as one of the best salivary indicators for oral squamous cell carcinoma (OSCC), and detect (dl)-lactic acid in type 2 diabetes in order to diagnose Alzheimer's disease. [48]

Dried urine spot (DUS)

Depending on the situation, it has been expected that DUS will lower the costs of handling, specimen collection, storage, and transportation for therapeutic research. [49] This method makes it possible to detect drugs of abuse using many analytes in dried urine specimens. DUS validated the rise in methylcitrate, a biochemical marker of inherited flaws in propionate metabolism. [50] Titanium, molybdenum and organophosphate pesticides as well as neuroleptics, antidepressants, cardiovascular drugs, opioids, benzodiazepines and stimulants can all be detected with DUS in urine samples. [51]

RESTRICTED ACCESS MEDIA

Another method makes use of normal laminar flow liquid chromatography to enable direct injection of plasma or serum into the chromatographic system while it is running. The RAM particles packed within columns are designed to inhibit or restrict the passage of large macromolecules to the interior adsorption sites of the bonded phase. Internal Surface Reversed Phase (ISRP) is the most widely utilised RAM column in bioanalysis (ISRP). The exterior particle surface of this type of column is covered with a non-adsorptive yet hydrophilic substance, and the internal particle surface (pore) is coated with a bonded reversed phase material. The sample matrix macromolecules and the target analyte are successfully separated by this dual-phase column. Proteins and bigger matrix elements are rejected whereas drugs and other tiny molecules pass through the hydrophobic reversed phase holes to partition andretain.

The biological sample matrix can be directly injected onto the column as dual-phase structureof the RAM materials allows it; little or no preparation is necessary. Retention time for RAM columns can be very long (over 10 min), washing the column between injections is necessary, and necessary mobile phases aren't necessarily compatible with all ionisation procedures usedin LC-MS/MS. Techniquesfor dualcolumn RAM arealso employed. These methods employ a column connected in series after the RAM column and used for analytical separation.

Advantages: i. High repeatability, ii. Good clean-up ability.

Disadvantages: i. Relatively long extraction time, ii. Limited solvent choice.

MICROEXTRACTION BY PACKED SORBENT (MEPS

This extraction method exhibits a number of very intriguing potential advantages, including low solvent consumption, small sample volumes (10–50 uL), and the capability to be directly injected into the HPLC system without additional treatments. Solvent volumes are also compatible with a variety of instrument configurations and analyses.

This device is employed in a variety of industries, including biological applications . The biggest disadvantage is also connected to its benefits. Its use in analyses where only small quantities are available, like plasma, is actually made possible by the ability to use small sample volumes.

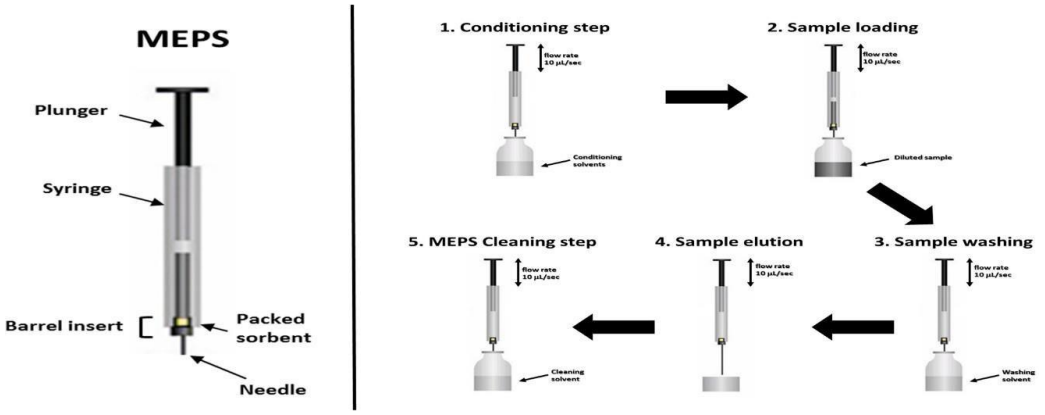

Figure 3 Device (left) and general procedure (right) applied in MEPS extraction.

There are several different types of packing materials available today, including: Silica-based sorbents SIL (unmodified silica), C2 (ethyl), C8 (octyl), and C18 (octadecyl); Mixed-mode C8 and ion exchange (SCX), Mixed-mode M1 (80% C8 and 20% SCX with sulfonic acid linked silica); PS-DVB (polystyrene-divinylbenzene), porous graphitic carbon Monoclonal antibodies (mAbs) for the creation of immunoaffinity sorbents are examples of molecular imprinted polymers (MIPs) based on various templates. [52] ,[53]

Advantages: i) Cheap, ii) Easy to automate, iii) Miniaturise

Disadvantages: i) Possibilityof fibreporesgettingblock, iii)Lowselectivityandprecision

CONCLUSION

Bioanalysis are crucial to support drug discovery and are used to analyse metabolites and biomarkers. The most frequent biological sample matrices used in bioanalysis are plasma, urine, and cerebrospinal fluid. Techniques for sample preparation in bioanalysis make it possible to extract and enrich important molecules that are present in complicated matrices at extremely low quantities. Biologicalapplication extractionprocedures areselective enough to retain and identify the target analyte from diverse samples when detection

techniques are used. Numerous interesting methods for preparing bioanalytical sample are identified in the current review, including HF-LPME, EME, DLLME, SPME and SBSME. The salient characteristics of various sample preparation methods are outlined. Modern sample preparation methods have been shown to be more accurate, well-liked, and practical than older methods.

ACKNOWLEDGMENTS

The authors thank SMBT College of Pharmacy for providing thenecessary facilities to conduct this review.

DECLARATIONS

Authors' contributions

All authors contributed equally to the design, execution, and interpretation of the research, as well as the drafting and revision of the manuscript. All authors approved the final version of the manuscript and are responsible for its content

Conflict of interest

All authors declare no conflicts of interest.

Ethical approvals

(Institutional ethical approvals and informed consent)

REFERENCES

1. Moein MM, Beqqali AE, Abdel-Rehim, M. Bioanalytical method development and validation: Critical concepts and strategies. J of Chromatography B. 2017;1043:3–11. 27720355. Available from: https://pubmed.ncbi.nlm.nih.gov/27720355/. 10.1016/j.jchromb.2016.09.028.
2. Ashri NY, Abdel-Rehim, M. Sample treatment based on extraction techniques in biological matrices. Bioanalysis. 2011;3:2003–2018. 21899508. Available from: https://pubmed.ncbi.nlm.nih.gov/21899508/. 10.4155/bio.11.201.
3. Vaghela A, Patel A. Samplepreparationinbioanalysis: Areview. INTERNATIONAL JOURNAL OF SCIENTIFIC & TECHNOLOGY RESEARCH. 2016;5(5):6–10. Available from: https://www.ijstr.org/final-print/may2016/Sample-Preparation-In-Bioanalysis-A-Review.pdf.
4. Kohler I, Guillarme D. Multi-target screening of biological samples using LC-MS/MS: focus on chromatographic innovations. Bioanalysis. 2014;6:1255– 1273. 24946925. Available from: https://pubmed.ncbi.nlm.nih.gov/24946925/.

10.4155/bio.14.80.

5. Lopes BR, Barreiro JC, Cass QB. Bioanalytical challenge: A review of environmental and pharmaceuticals contaminants in human milk. J Pharm Biomed Anal. 2016;130:318–325. 27372148. Available from: https://pubmed.ncbi.nlm.nih.gov/27372148/. 10.1016/j.jpba.2016.06.012.
6. Buszewski B, Szultka M. Past present and future of solid phase extraction: A review. Crit Rev Anal Chem. 2012;42:198–213.
7. Alexovic M, Dotsikas Y, Bober P. Achievements in robotic automation of solvent extraction and related approaches for bioanalysis of pharmaceuti- cals. J of Chromatography B Analyt Technol Biomed Life Sci. 2018;1092:402–421. 29945105. Available from: https://pubmed.ncbi.nlm.nih.gov/29945105/. 10.1016/j.jchromb.2018.06.037.
8. Arthur CL, Pawliszyn J. Solid-phase microextraction with thermal desorption using fused silica optical fiber. Anal Chem. 1990;62:2145–2148. Available from: https://pubs.acs.org/doi/10.1021/ac00218a019.
9. Boyaci E, Rodríguez LA, Gorynski K. Samplepreparation with solid phase microextraction and exhaustive extraction approaches: comparison for challenging cases. Anal Chim Acta. 2015;873:14–30. 25911426. Available from: https://pubmed.ncbi.nlm.nih.gov/25911426/. 10.1016/j.aca.2014.12.051.
10. Galievsky V,Pawliszyn J. Fluorometer for screening of doxorubicininperfusatesolution and tissue with solid-phase microextraction chemical biopsy sampling. Anal Chem. 2020;92:13025–13033. 15039931. Availablefrom: https://pubmed.ncbi.nlm.nih.gov/15039931/. 10.1002/jms.606.
11. Liu H, Dasgupta PK. Analytical chemistry in a drop solvent extraction in a microdrop. Anal Chem. 1996;68:1817–1821. 32847350. Available from: https://pubmed.ncbi.nlm.nih.gov/32847350/. 10.1021/acs.analchem.0c01905.
12. Liu H, Dasgupta PK. Analytical chemistry in a drop. Solvent extraction in a microdrop. NIH NLM;21619093. Available from: https://pubmed.ncbi.nlm.nih.gov/21619093/. 10.1021/ac960145h.
13. Filippou O, Bitas D, Samanidou V. Green approaches in sample preparation of bioanalytical samples prior to chromatographic analysis. J Chromatogr B Ana- lyt Technol Biomed Life Sci. 2017;1043:44–62. 27623110. Available from: https://pubmed.ncbi.nlm.nih.gov/27623110/. 0.1016/j.jchromb.2016.08.040.
14. Jeannot MA, Cantwell FF. Solvent microextraction into a single drop. Anal Chem. 1996;68:2236–2240. 21619310. Available from: https://pubmed.ncbi.nlm.nih.gov/21619310/. 10.1021/ac960042z.
15. Ochiai N, Sasamoto K, David F. Solvent-assisted stir bar sorptive extraction by using swollen polydimethylsiloxane for enhanced recovery of polar solutes in aqueous samples: application to aroma compounds in beer and pesticides in wine. J Chromatogr A. 2016;1455:45–56. 27289502. Available from: https://pubmed.ncbi.nlm.nih.gov/27289502/. 10.1016/j.chroma.2016.05.085.
16. He M, Wang Y, Zhang Q. Stir bar sorptive extraction and its application. J Chromatogr A. 2021;1637:461810–461810.
17. Clark KD, Zhang C, Anderson JL. Sample preparation for bioanalytical and pharmaceuticalanalysis. Anal Chem. 2016;88:11262–11270. 27779849. Availablefrom:

https://pubmed.ncbi.nlm.nih.gov/27779849/. 10.1021/acs.analchem.6b02935.

18. Campillo N, Vinas P, Sandrejova J, Andruch V. Ten years of dispersive liquid-liquid microextraction and derived techniques. Appl Spectrosc Rev. 2017;52:267–415. Available from: https://colab.ws/articles/10.1080/05704928.2016.1224240. 10.1080/05704928.2016.1224240.
19. Yilmaz E, Soylak M. Latest trends green aspects and innovations in liquid-phase-based microextraction techniques: A review. Turkish J Chem. 2016;40:868–893. Available from: https://journals.tubitak.gov.tr/chem/vol40/iss6/2/. 10.3906/kim-1605-26.
20. Diuzheva A, Carradori S, Andruch V, Locatelli M, De LE, Tiecco M, et al. Use of innovative (micro)extraction techniques to characterize harpagophytum procumbens root and its commercial food supplements. Phytochem Anal. 2018;29(3):233–241.
21. Mansour FR, Danielson ND. Solidification of floating organic droplet in dispersive liquid liquid microextraction as a green analytical tool. Talanta. 2017;170:22–35. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0039914017303818. https://doi.org/10.1016/j.talanta.2017.03.084.
22. Zhao Y, Hou X, Qin D. Dispersive liquid-liquid microextraction method for the simultaneous determination of four isomers of hexa-chlorocyclohexane and six pyrethroid pesticides in milk by gas chromatography electron capture detector. Food Anal Methods. 2020;13:370–381. 10.1007/s12161-019-01662-w.
23. Asati A, Satyanarayana G, Patel DK. Comparison of two microextraction methods based on solidification of floating organic droplet for the determination of multiclass analytes in river water samples by liquid chromatography tandem mass spectrometry using Central Composite Design. J Chromatogr A. 2017;1513:157–171.
24. Ferrone V, Cotellese R, Carlucci M. Air assisted dispersive liquid-liquid microextraction with solidification of the floating organic droplets (AA-DLLME-SFO) and UHPLC-PDA method: application to antibiotics analysis in human plasma of hospital acquired pneumonia patients. J Pharm Biomed Anal. 2018;151:266–273. Availablefrom: https://www.sciencedirect.com/science/article/abs/pii/S0731708517319830. https://doi.org/10.1016/j.jpba.2017.12.039.
25. Kiarostami V, Rouini MR, Mohammadian R. Binary solvents dispersive liquid-liquid microextraction (BS-DLLME) method for determination of tramadol in urine using high-performance liquid chromatography. DARU J Pharm Sci. 2014;22:25–25. 24495475. Available from: https://pubmed.ncbi.nlm.nih.gov/24495475/. 10.1186/2008-2231-22-25.
26. Pedersen BS, Rasmussen KE. Recovery, enrichment and selectivity in liquid-phase microextraction-comparison with conventional liquid-liquid extraction. J Chromatogr A. 2002;963(1-2):3–17. 12187984. Available from: https://pubmed.ncbi.nlm.nih.gov/12187984/. 10.1016/s0021-9673(02)00215-7.
27. Pedersen BS, Rasmussen KE. Electrokinetic migration across artificial liquid membranes - new concept for rapid sample preparation of biological fluids. J Chromatogr A. 2006;1109(2):183–190. 16445928. Availablefrom: https://pubmed.ncbi.nlm.nih.gov/16445928/. 10.1016/j.chroma.2006.01.025.

28. Morales C, Cardenas S, Simonet BM, Valcarcel M. Sample treatments improved by electric fields. Analyt Trend Anal Chem. 2010;29(2):158–165.
29. Kuban P, Slampova A, Bocek P. Electric field-enhanced transport across phase boundaries and membranes and its potential use in sample pretreatment for bio-analysis. Electrophoresis. 2010;31(5):768–785. 20191542. Available from: https://pubmed.ncbi.nlm.nih.gov/20191542/. 10.1002/elps.200900561.
30. Yan J, Kuzhiumparambil U, Bandodkar S. Development and validation of a simple rapid and sensitive LC-MS/MS method for the measurement of urinary neurotransmitters and their metabolites. Anal Bioanal Chem. 2017;409:7191–7199. 29030665.

Available from: https://pubmed.ncbi.nlm.nih.gov/29030665/. 10.1007/s00216-017-0681-3.
31. Yu X, Li X, You S. Electromembrane extraction of chlorprothixene, haloperidol and risperidone from whole blood and urine. J Chromatogr A. 2020;1629:461480–461480. 32827905. Available from: https://pubmed.ncbi.nlm.nih.gov/32827905/. 10.1016/j.chroma.2020.461480.
32. Venson R, Korb AS, Cooper G. A review of the application of hollow-fiber liquid-phase microextraction in bioanalytical methods-a systematic approach with focus on forensic toxicology. J Chromatogr B Analyt Technol Biomed Life Sci. 2019;1108:32–53. 30682538. Available from: https://pubmed.ncbi.nlm.nih.gov/30682538/. 10.1016/j.jchromb.2019.01.006.
33. Shukri D, Sanagi MM, Ibrahim W. Liquid chromatographic determination of NSAIDs in urine after dispersive liquid-liquid microextraction based on solidification of floating organic droplets. Chromatographia. 2015;78:987–994. 10.1007/s10337-015-2920-0.
34. Arain SS, Kazi TG, Arain JB. Preconcentration of toxic elements in artificial saliva extract of different smokeless tobacco products by dual-cloud point extraction. Microchem J. 2014;112:42–49. 23566880. Availablefrom: https://pubmed.ncbi.nlm.nih.gov/23566880/. 10.1016/j.ecoenv.2013.03.001.
35. Li N, Zhang T, Chen G. Recent advances in sample preparation techniques for quantitative detection of pharmaceuticals in biological samples. TrACTrends Anal Chem. 2021;142:116318–116318.
36. Olcer YA, Tascon M, Eroglu AE. Thin film microextraction: towards faster and more sensitive microextraction. TrAC Trends Anal Chem. 2019;113:93–101. Available from: https://open.metu.edu.tr/handle/11511/48426. https://doi.org/10.1016/j.trac.2019.01.022.
37. El-Sherbeni AA, Stocco MR, Wadji FB. Addressing the instability issueof dopamine during microdialysis: the determination of dopamine serotonin methamphetamine and its metabolites in rat brain. J Chromarogr A. 2020;1627:461403–461403. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7484461/.
38. Chepyala D, Kuo HC, Su KY. Improved dried blood spot-based metabolomics analysis by a postcolumn infused-internal standard assisted liquid chromatography-electrospray ionization mass spectrometry method. Anal Chem. 2019;91:10702–10712. Available from: https://pubmed.ncbi.nlm.nih.gov/31361473/.
39. Nys G, Kok M, Servais AC. Beyond dried blood spot: current microsampling

techniques in the context of biomedical applications. TrAC Trends Anal Chem. 2017;97:326–332. 10.1016/j.trac.2017.10.002.

40. Capiau S, Veenhof H, Koster RA. Official International Association for Therapeutic Drug Monitoring and Clinical Toxicology Guideline: development and validation of dried blood spot-based methods for therapeutic drug monitoring. Ther Drug Monit. 2019;41:409–430. 31268966. Available from: https://pubmed.ncbi.nlm.nih.gov/31268966/. 10.1097/FTD.0000000000000643.

41. Lombardi V, Carassiti D, Giovannoni G. The potential of neurofilaments analysis usingdry-bloodandplasma spots. Sci Rep. 2020;10:97–97. PMC6952412. Available from: https://pubmed.ncbi.nlm.nih.gov/31919375/.10.1038/s41598-019-54310-y.

42. Parker SL, Lipman J, Dimopoulos G. A validated method for the quantifi- cation of fosfomycin on dried plasma spots by HPLC-MS/MS: application to a pilot pharmacokinetic study in humans. J Pharm Biomed Anal. 2020;115:509–514. 26299527. Available from: https://pubmed.ncbi.nlm.nih.gov/26299527/. 10.1016/j.jpba.2015.07.013.

43. Li W,Doherty J,Favara S. Evaluation of plasma microsamplingfor driedplasma spots (DPS) in quantitative LC-MS/MS bioanalysis using ritonavir as a model compound. JChromatogr BAnalTechnolBiomedLifeSci. 2015;991:46–52. 25913423. Available from: https://pubmed.ncbi.nlm.nih.gov/25913423/. 10.1016/j.jchromb.2015.03.026.

44. Gonzalez D, Melloni C, Poindexter BB. Simultaneous determination of trimetho-prim and sulfamethoxazole in dried plasma and urine spots. Bioanalysis. 2015;7:1137–1149. 23566880. Available from: https://pubmed.ncbi.nlm.nih.gov/26039810/. 10.1016/j.ecoenv.2013.03.001.

45. Meesters R, Hooff G, Van Huizen N. Impact of internal standard addition on dried bloodspot analysis inbioanalytical methoddevelopment. Bioanalysis. 2011;3:2357–2364. 22011183. Available from: https://pubmed.ncbi.nlm.nih.gov/22011183/. 10.4155/bio.11.202.

46. Zheng N, Zeng J, Ji QC. Bioanalysis of dried saliva spot (DSS) samples using detergent-assisted sample extraction with UHPLC-MS/MS detection. Anal Chim Acta. 2016;934:170–179. 27506357. Available from: https://pubmed.ncbi.nlm.nih.gov/27506357/. 10.1016/j.aca.2016.05.057.

47. Hsiao YC, Lin SY, Chien K. An immuno-MALDI mass spectrometry assay for the oral cancer biomarker, matrix metalloproteinase-1, in dried saliva spot samples. Anal Chim Acta. 2020;1100:118–130. 31987131. Available from: https://pubmed.ncbi.nlm.nih.gov/31987131/. 10.1016/j.aca.2019.12.006.

48. Numako M, Toyo'oka T, Noge I. Risk assessment of diabetes mellitus using dried saliva spot followed by ultra-performance liquid chromatography with fluorescence and mass spectrometry. Microchem J. 2018;142:202–207. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0026265X18304107. https://doi.org/10.1016/j.microc.2018.06.037.

49. Pablo A, Breaud AR, Clarke W. Automated analysis of dried urine spot (DUS) samples for toxicology screening. Clin Biochem. 2020;75:70–77. 31707014. Available from: https://pubmed.ncbi.nlm.nih.gov/31707014/. 10.1016/j.clinbiochem.2019.10.009.

50. Dhahouri A, Langhans N, D C, Hammadi A, Z. Quantification of methylci- trate in dried urine spots by liquid chromatography tandem mass spectrometry for the diagnosis of propionic and methylmalonic acidemias. Clin Chim Acta. 2018;487:41–45. 30217751. Available from: https://pubmed.ncbi.nlm.nih.gov/30217751/. 10.1016/j.cca.2018.09.017.

51. Kok M, Fillet M. Volumetric absorptive microsampling: current advances and applications. J Pharm Biomed Anal. 2018;147:288–296. 28803682. Available from: https://pubmed.ncbi.nlm.nih.gov/28803682/. 10.1016/j.jpba.2017.07.029.

52. Iskierko Z, Sharma PS, Prochowicz D, Fronc K, Souza D, Toczydłowska F, et al. Molecularly Imprinted Polymer (MIP) Film with Improved Surface Area Developed by Using Metal-Organic Framework (MOF) for Sensitive Lipocalin (NGAL) Determination. ACS Appl Mater Interfaces. 2016;8:19860–19865. Available from: https://pubs.acs.org/doi/abs/10.1021/acsami.6b05515.

53. Qian K, Fang G, Wang S. A novel core-shell molecularly imprinted polymer based on metal-organic frameworks as a matrix. Chem Commun. 2011;47:10118–10120. Available from: https://pubs.rsc.org/en/content/articlelanding/2011/cc/c1cc12935j