SurFACTS in Biomaterials

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INSIDE THIS ISSUE

From President Landon Nash

Welcome to the Summer 2023 edition of the Surfaces in Biomaterials SurFACTS newsletter! This is my last letter as the Surfaces in Biomaterials Foundation (SIBF) President, but my commitments to this organization will be career-long. It has been a privilege to serve the foundation and advocate for the interests of our supporting membership. I have been involved with this organization since I was a graduate student, and it continues to be one of my favorite venues for technical collaboration and inspiration.

Finishing touches are being finalized for our annual conference, the 2023 BioInterface Workshop and Symposium at the Catamaran Resort in San Diego, Monday 9/25/23 - Wednesday 9/27/23. Please visit our website at surfaces.org to view the recently released conference program and register for the event.

The entire SIBF Board and conference planning committee look forward to seeing everyone in person to network, discuss surface science, and galvanize relationships between industry and academic partners interested in the fields of biomaterials and medical devices.

Like many small non-profit organizations, the Foundation has endured many headwinds over the past several years, many resulting from the COVID-19 pandemic. Despite these challenges, I am excited and hopeful about the trajectory of the organization. On behalf of the entire Surfaces in Biomaterials Foundation, we appreciate your continued commitment to our community, and we look forward to your continued engagement in 2023 and beyond. Please stay tuned for future SurFACTS newsletters, BioInterface 2023 updates, and other SIBF events.

Engineered Collagen-Glycosaminoglycans Scaffolds and their Application on Trabecular Meshwork and Glaucoma Studies

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Glaucoma impacts 80 million people globally and its prevalence is expected to double in the next two decades due to a constantly ageing population.[1] Elevation of intraocular pressure (IOP) due to inadequate drainage of aqueous humor (AH) is regarded as the primary and only modifiable risk factor for the most common form of glaucoma, primary open angle glaucoma (POAG). Trabecular meshwork (TM), a specialized filtering tissue located in the anterior chamber of the eye that provides resistance to AH drainage is the major determinant of IOP. Up to 85-90% of AH exits through the TM and Schlemm's canal, collectively called the conventional outflow pathway.[2] However, studies of TM cell behavior and its exact role in AH outflow is challenging due to the complex nature of the tissue. Moreover, the translation of findings from traditional tissue culture (TC) studies to in vivo environment is largely inconsistent, animal/human donor eyes are expensive to obtain and cumbersome to work with, and the TM varies among species making research more challenging.[3] Thus, there is an unmet need of a physiological mimic of human TM that improves the capability of TM cell studies and provides possible drug development platforms.

To achieve this, we have engineered biomaterial models using collagen (CO) and glycosaminoglycans (GAGs). CO and GAGs were selected as building blocks based on their abundance and roles in the TM extracellular matrix. Scaffolds were fabricated by uniaxially freezing molded slurries at various temperatures (-80 C or liquid N 2) depending on the desired pore dimensions. Freezing at cryo conditions (-196 C/ liquid N 2) resulted in scaffolds with smaller pores as compared to freezing at -80 C **(Fig 1A)**.[4,5] Furthermore, GAGs: hyaluronic acid (HA), chondroitin sulfate (CS) or a combination of both were added in the slurries to increase the complexity of the scaffolds for a better mimic of the trabecular meshwork. Once fabricated, properties such as retention of GAGs, cell proliferation and expression of extracellular matrix proteins were quantified. Scaffolds containing non-aligned large pores (NA80) supported highest proliferation and expression of FN gene by hTM cells for up to 4 weeks of culture. Furthermore, our results demonstrated a fibronectin fibrillar meshwork, which was more densely packed when the pores were aligned, and even more so when they were aligned and small in size, when compared to the other architectures **(Fig 1B)**.[5]

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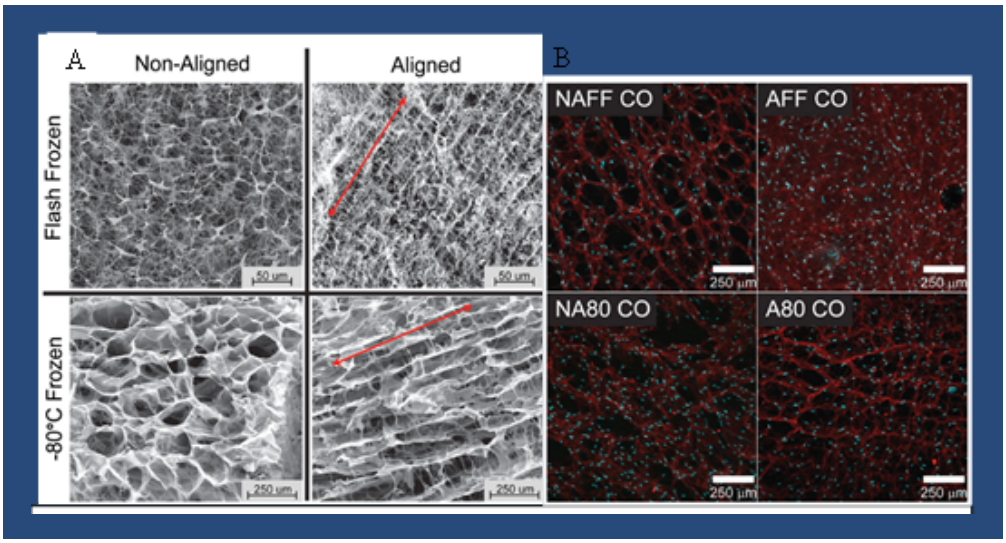

Figure 1:
(A) Scanning electron micrographs of the four types of scaffolds. Scaffolds were frozen in non-aligned and aligned configurations at -196°C
or -80°C. Red arrows indicate the direction of the pore alignment. Scale bars represent 50 µm for the flash frozen scaffolds and 250 µm for the -80°C frozen scaffolds.
(B) Confocal micrographs of collagen-only scaffolds after week 2 of culture. Fibronectin (red) and nuclei (blue). AFF, aligned flash frozen; CO, collagen only; NAFF, nonaligned flash frozen.

Cell cultures in NA80 scaffolds were further studied to understand the roles of GAGs in normal and dexamethasone (dex) induced conditions. Dex is a synthetic glucocorticoid that produces iatrogenic hypertension in patients and is commonly used in cell cultures toánduce glaucomatous phenotype in TM cells. Throughout this study, quantitative real time PCR (qPCR) and confocal microscopy were utilized to study the gene and protein expression of elastin, laminin, and MMP-2 under normal and dex induced culture conditions.

Elastin provides structural integrity to tissues against various forms of strain over a lifetime and thus is integral part of many ECMs. Laminins are proteins of the basement membrane that influence cell behavior by mediating communication between cells and the extracellular environment.

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Matrix metalloproteinases (MMPs) are proteolytic enzymes that play a role in ECM homeostasis by degrading various proteins and glycoproteins. Our findings suggest that culture conditions (TC vs scaffolds) and CS, HA affect the expression of ELN, LAM1 and MMP-2 genes in healthy TM cells **(Fig 2)**.[7] Overall, cells in 3D cultures express significantly higher levels of ELN and LAM genes as compared to cells in monolayer TC. CS upregulates hTM cells' expression of ELN gene by providing anchoring moiety to the cells which are important in its expression in vivo. HA, which lacks the anchoring galactose moiety, still upregulated the expression of elastin but not to the same extent as CS.

LAM on the other hand was affected by GAGs in a concentration dependent manner, with cells in scaffold containing 0.5% CS or HA expressing significantly higher amounts of LAM compared to those with half of each. The presence of GAGs in the culture microenvironment causes significant increase in the expression of MMP-2 mRNA. It is likely that this behavior is correlated since MMPs have been shown to be regulated by tissue inhibitors of MMPs (TIMPs) and GAGs.[8]

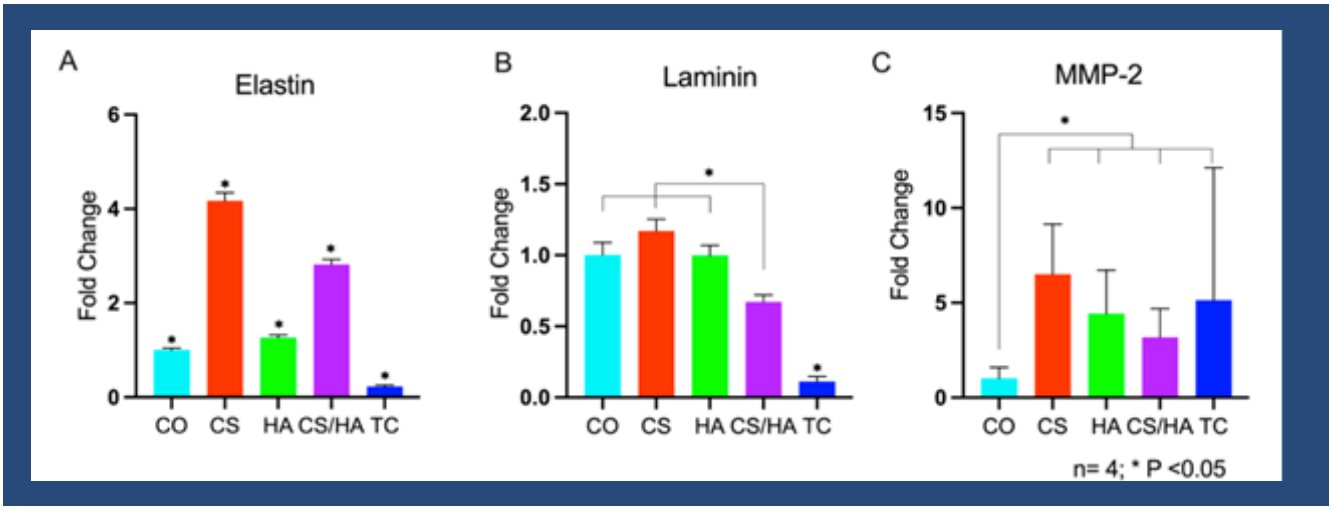

Figure 2: Relative expression levels of elastin (A), laminin (B), and MMP-2 (C) mRNA by hTM cells cultured in 3D collagen-GAG scaffolds for 2 weeks. Fold change was normalized to expression levels on collagen-only scaffolds.CO: Collagen; CS: Collagen +Chondroitin Sulfate; HA: Collagen +Hyaluronic acid; CS/HA: Collagen +Chondroitin Sulfate and Hyaluronic Acid; TC: Tissue culture plate. *p <0.05.

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hTM cells in dex induced cultures displayed some interesting findings. Although expressed in a smaller amount compared to normal conditions (-dex), laminin proteins are aggregated around the nuclei in dex induced cultures **(Fig 3)**.[7] We observed that the presence of GAGs causes laminin proteins to be localized away from the nuclei into the extracellular space and take a filamentous shape **(Fig 3C top)**. The action of dex on hTM cells' laminin production in 3D cultures is consistent regardless of scaffold composition as far as the protein morphology is concerned. These changes are paralleled by a shift from filamentous to clustered granular organization of laminin molecules revealed immunocytochemically **(Fig 3C bottom)**. It is plausible that dex induction causes these proteins to form clusters via protein-protein interactions aggregating them around the nucleus, resulting in diminished laminin proteins in the basement membrane, which may lead to increased susceptibility to stress causing damage to the cells. Further studies are necessary to fully understand the mechanism of laminin clustering and its effects on cell behavior in relation to glaucomatous phenotype.

Our model is exciting and attractive to professionals in early stage of drug development against POAG. These easily reproducible systems can be employed in numerous studies of the trabecular meshwork cell behavior and aid in drug development efforts while cutting the direct and indirect cost of animal studies.

For example, our hTM model can be deployed to study expression and physiological turnover of the TM ECM in relation to numerous critical proteins. Furthermore, this model opens countless possibilities for understanding the relatively unknown hTM cell behavior in physiological and glaucomatous states.

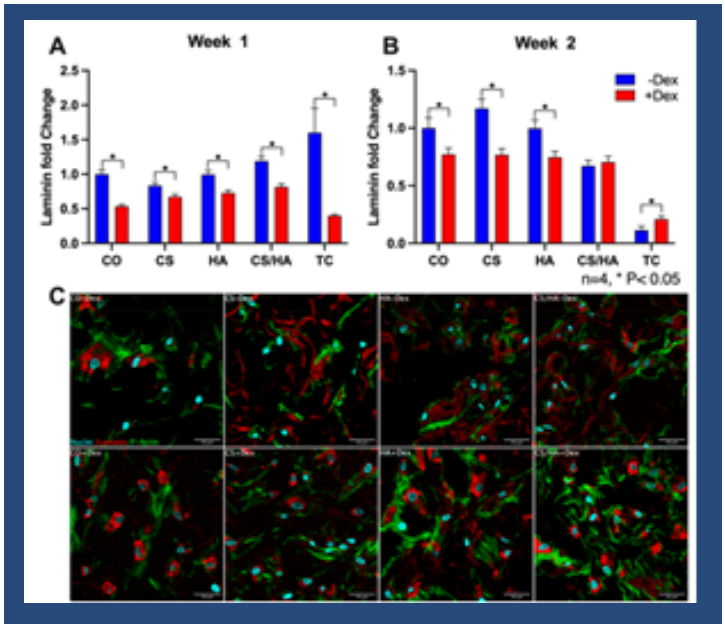

Figure 3: Fold change expression levels of laminin cultured on CO-GAG scaffolds for 1week (A) and 2weeks (B) in the absence (blue) and presence (red) of 100 nM dex. (C) Confocal images of cell laden scaffolds after 2weeks of culture in the absence (top) and presence (bottom) of dex. The constructs were stained for laminin (red), F-actin (green), and cell nuclei (blue) and imaged at 40X magnifications. Scale bars represent 50mm, and * signifies p <0.05.

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References:

1. Tham, Y.-C. et al. Global Prevalence of Glaucoma and Projections of Glaucoma Burden through 2040: A Systematic Review and Meta-Analysis. Ophthalmology 121, 2081–2090 (2014).

2. Johnson, M. What controls aqueous humour outflow resistance? Exp. Eye Res. 82, 545–557 (2006).

3. Chen, L., Zhao, Y. & Zhang, H. Comparative Anatomy of the Trabecular Meshwork, the Optic Nerve Head and the Inner Retina in Rodent and Primate Models Used for Glaucoma Research. Vision 1, 4 (2016).

4. Osmond, M., Bernier, S. M., Pantcheva, M. B. & Krebs, M. D. Collagen and collagen-chondroitin sulfate scaffolds with uniaxially aligned pores for the biomimetic, three dimensional culture of trabecular meshwork cells. Biotechnol. Bioeng. 114, 915–923 (2017).

5. Osmond, M. J., Krebs, M. D. & Pantcheva, M. B. Human trabecular meshwork cell behavior is influenced by collagen scaffold pore architecture and glycosaminoglycan composition. Biotechnol. Bioeng. 117, 3150–3159 (2020).

6. Overby, D. R. & Clark, A. F. Animal models of glucocorticoid-induced glaucoma. Exp. Eye Res. 141, 15–22 (2015).

7. Adhikari, B., Osmond, M. J., Pantcheva, M. B. & Krebs, M. D. Glycosaminoglycans Influence Extracellular Matrix of Human Trabecular Meshwork Cells Cultured on 3D Scaffolds. ACS Biomater. Sci. Eng. 8, 5221–5232 (2022).

8. Ruiz-Gómez, G., Vogel, S., Möller, S., Pisabarro, M. T. & Hempel, U. Glycosaminoglycans influence enzyme activity of MMP2 and MMP2/TIMP3 complex formation – Insights at cellular and molecular level. Sci. Rep. 9, 4905 (2019).

Agonies and Thrills of Chemical Characterization of Extractables of Medical Devices

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Abstract

This article highlights the shortfalls of solvent extract analysis by all platforms, as routinely performed by the industry, to comply with FDA requirements for chemical characterization of medical device extractables. The article provides recommendations for streamlining the study design to reduce generation of questionable and incompatible data that wastes resources and increases cost. Also, there are recommendations for performing selective analysis to improve detection of potential compounds of toxicological concern which otherwise go undetected by general screening. The recommendations are based on fundamental principles of chemistry, predominance of analytes solubility in the extraction solvent, instrument selectivity, and review of results from numerous analytical reports for different medical devices from various laboratories.

Introduction

Numerous articles have been published about chemical characterization of medical device solvent extracts to ensure safe, intended use following ISO guidelines.[1,2] None of the published articles discussed the benefits of analysis of all solvent extracts, by all platforms, routinely requested by the industry as part of chemical characterization of medical devices. ISO 10993-18 states: "*The extracts shall be analysed using sensitive and selective methods to screen the extracts for extractables, and the detected extractables above the analytical evaluation threshold (AET).*" However, the FDA does not accept selective analysis and requires analysis by all platforms, as indicated by the following FDA audit statement: "*FDA does not accept selective analysis and all extracts should be analyzed by all platforms.*" The requirements by FDA for analysis of all extracts, by all platforms, requires additional sample preparation and analysis resulting in lack of data corroboration, waste of resources, and higher costs, which often leads to inaccurate results used for evaluation of toxicological risk assessment.

The question is what are the benefits of analysis of polar extracts by Gas Chromatography Mass Spectrometry (GCMS) and nonpolar extracts by Liquid Chromatography Mass spectrometry (LCMS), when the semi-polar solvent extracts has already filled any extraction or detection gap by the direct analysis on GCMS and LCMS?

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General Chemical Characterization

Chemical characterization is generally performed on extracts of small molecules in a suitable solvent following four basic criteria:

a) Solvent compatibility with the device construction materials.
b) Solvent extraction efficiency to ensure the highest concentration of analytes for detection above the Analytical Evaluation Threshold (AET).
c) Solvent inertness with the extracted analytes.
d) Determination and toxicological risk assessment of parent extractable compounds of reported reactive products.

Most study designs emphasize solvent compatibility with the device but tend to overlook solvent inertness with extracted analytes.[3-5] Also, most laboratories use three different solvents for extraction in line with FDA requirements to ensure extraction of analytes at highest concentration, a preferred analytical approach for detection of analytes at low level. In addition, all laboratories report reaction products of reactive extractables for toxicological risk assessment.

Reviews of laboratory data show that various study designs and analytical reports include a description of analysis by all platforms as described below:

- GCMS: For analysis of volatiles (VOCs) and semi-volatile organic compounds (SOVCs) in non-polar, semi-polar and polar extracts.
- UPLCUVMS: For analysis of semi-volatiles (SOVCs) and non-volatile organics (NVOCs) compounds in polar, semi-polar and non-polar extracts.
- HS/GCMS of polar solvent extracts for analysis of VOCs.
- ICP/MS: For analysis of trace metals and elemental impurities in aqueous extracts.

ISO 10993-18 guidelines also states: "*Organic extractables can be qualitatively placed into three classes based on their volatility; VOC, SVOC and NVOC. The analytical techniques used to screen for these classes of organic extractables are different, though one chemical can often be detected using a variety of techniques; for example, gas chromatography with headspace sampling (HS-GC) is typically used to analyse VOCs, gas chromatography (GC) is typically used to analyse SVOCs and LC is used to analyse NVOCs.*"

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This statement emphasizes the use of selective and sensitive technique for analysis of each class of extracts as shown graphically in Figure 1. Figure 1 also describes the solubility/extractability of compounds based on -- solvent polarity. Figure 2 show the selective instrument for the analysis of specific solvent extracts or class of compounds. Analysis of compounds barely soluble in either polar or non-polar solvent would require multifold concentration to presumably bring AET above the limit of detection.

However, concentration of complex matrix extracts without further purification is not a recommended approach for analysis of complex extracts. *(6-9)*

The non-polar compounds described as volatiles (VOCs) and semi-volatiles (SVOCs) are predominantly soluble in non-polar solvents, and partially soluble in polar solvents. This class of compounds is selectively analyzed by direct injection on GCMS as described in Figure 2 and the ISO 10993-18 guidelines.

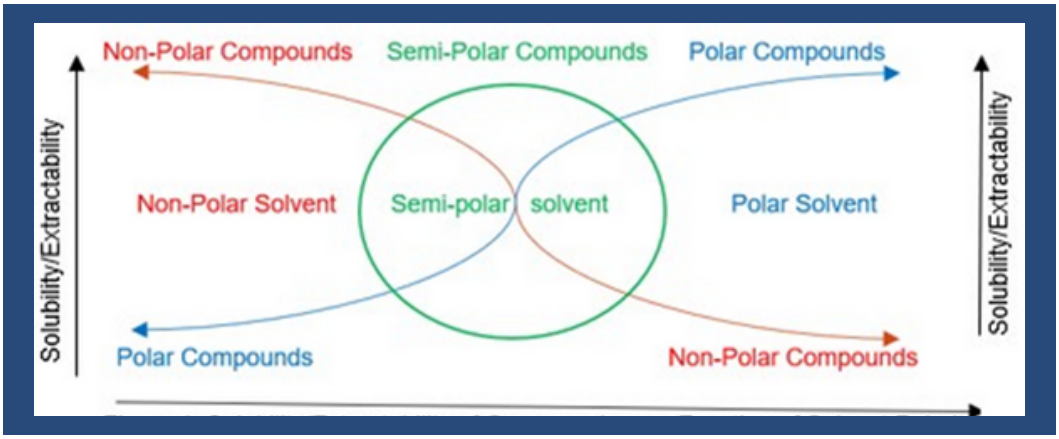

Figure 1: Solubility/Extractability of Compounds as a Function of Solent Polarity

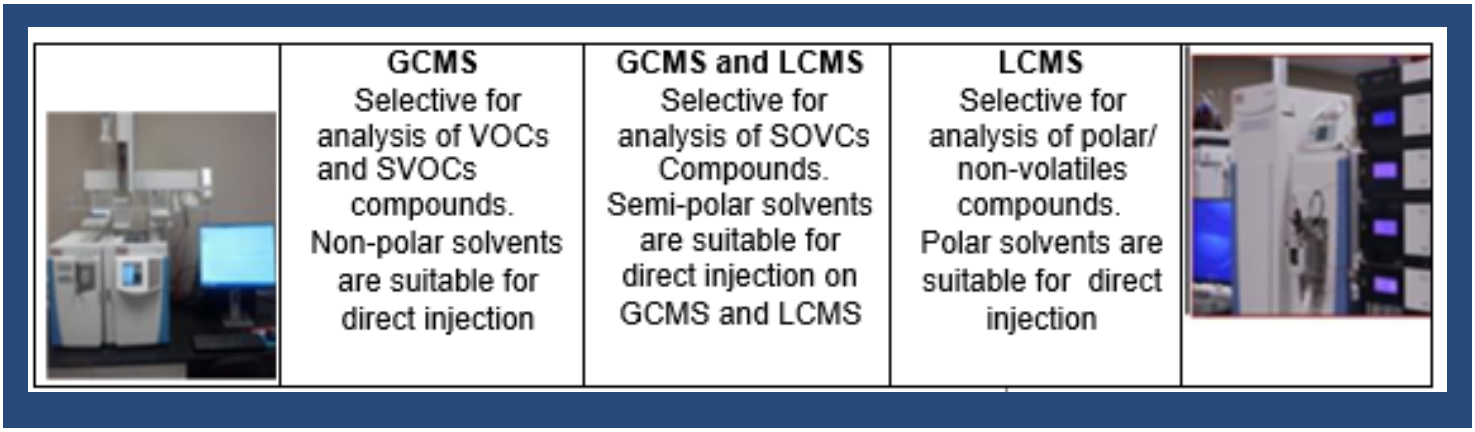

Figure 2: Instrument Selectivity of Analysis of Solvent Extracts

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The polar compounds described as non-volatiles (NVOCs) are predominantly soluble in polar solvents, and partially soluble in non-polar solvents. This class of compounds exhibits high polarity due to the presence of functional groups and/or electronegative atoms in their chemical structures. Examples of polar solvents are water, saline, and phosphate buffer, as indicated in ISO10993-18, Table D.1. They are easily ionized, and selectively analyzed by LCMS operating in electrospray ionization (ESI) either in positive or negative mode.

The semi-polar compounds are predominantly soluble in semi-polar solvents acting as a buffer zone between polar and nonpolar solvents. Semi-polar solvent extraction efficiency results in predominant extraction of semi-polar compounds which are partially soluble in polar and non-polar solvents. Examples of semi-polar solvents are described in ISO10993-18, Table D.1: dimethyl sulfoxide, acetonitrile, methanol, acetone, ethanol, tetrahydrofuran, n-propyl alcohol. These solvents are amenable for direct analysis by GCMS and LCMS.

Analytical Issues with Analysis of Polar Extracts by GCMS

To enable analysis of polar extracts by GCMS, we observed that most laboratories have issues with sample preparation resulting in less than optimum conditions for sample analysis. Some laboratories use direct injection of water extracts, others perform liquid-liquid extraction (LLE) using a non-miscible solvent such dichloromethane or hexane. Each of these techniques carries with it additional cost and analytical challenges.

Polar Extracts: Direct injection of aqueous extracts on GCMS is not recommended. High-quality GC/MS analysis requires a low, and stable background of air and water in the MS analyzer as determined by the tuning parameters. Also, aqueous extracts degrade the chromatographic column and may contain large amounts of soluble salts, inorganics, metal ions, etc., which are not volatiles and tend to deposit in the injection port and the tip of the column. These can lead to system failure, replacement of accessories, downtime, repeat analysis, and inconsistent results.

LLE Extracts: LLE extraction is demanding, labor intensive and time consuming. It requires the use of different glassware contributing to potential sample contamination. It also does not comply with good sample preparation for optimum analysis especially at trace levels. Liquid-liquid extraction from aqueous media results mainly in extraction of non-polar and semi polar compounds. These two classes of compounds are predominantly extracted either in non-polar or semi-polar solvents and analyzed by direct injection on GCMS and LCMS. In addition, the separated organic phase is injected without drying of residual water, as observed in most reports, carrying with it additional problems for GCMS analysis.

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In addition, some laboratories perform laborious LLE of aqueous extracts at different pHs: acidic, basic, and neutral. This is commonly used in separation and purification of acidic and basic compounds from aqueous extracts and enhances extraction of acidic and basic analytes. Extraction at different pH requires considerable time for sample preparation, analysis, and reporting. Re-extraction at different pHs is deemed not necessary for analysis by GCMS because polar extracts are directly analyzed by LCMS. Analysis by LCMS is more specific and selective for acidic and basic analytes. Analysis of polar compounds by GCMS often requires derivatization or chemical modifications. Liquid-liquid re-extraction at neutral pH results in poor to no recovery of polar and ionic compounds adding no value to direct injection and analysis of non-polar extracts on GCMS and semi-polar extracts on both GCMS and LCMS.

Analytical Issues with Analysis of Non-Polar Extracts by LCMS

Issues in sample preparation have also been observed for the analysis of non-polar (e.g., hexane) extracts by LCMS, resulting in less than optimum conditions for analysis. Analytical laboratories use different techniques for LCMS analysis: direct injection, dilution with IPA, or evaporation of the solvent followed by reconstitution of the residue using a compatible medium. Each of these techniques has analytical challenges and does not comply with good sample preparation for optimum analysis, especially at trace levels.

Direct injection of non-polar solvent is not recommended. Non-polar solvent is not compatible/miscible with the aqueous mobile phase commonly used for LCMS chromatographic separation for extractables.

Dilution with IPA is not a recommended option due to residual non-polar solvent in the sample and risk of contamination from non-polar soluble compounds such as oils, hydrocarbons of high molecular weight, lubricants, slipping agents, etc. These types of non-polar compounds are not soluble in aqueous mobile phase and are a source of contamination difficult to remove from the system. Also, non-polar solvents are not ionizable, a requirement for optimum ionization and detection by Electrospray Ionization (ESI).

Evaporation of non-polar extracts followed by reconstitution results in extraction of partially soluble, semi-polar compounds, because polar compounds are insoluble or partially soluble in non-polar solvents. Extraction of semi-polar compounds is more appropriate in semi-polar solvent, rendering insignificant the additional sample preparation required for LCMS analysis.

Recommendations

The FDA should reassess the requirement for analysis of all extracts by all platforms because selective analysis should apply to solvent extracts in which analytes are predominantly extracted.

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Polar solvents extract predominantly polar compounds, and LCMS is the selective instrument for analysis of this class of compounds. Non-polar compounds are selectively extracted in non-polar solvents, and this type of compounds is analyzed by GCMS. Semi-polar compounds are predominantly extracted in semipolar solvents, and this class of compounds are analyzed by both GCMS and LCMS bridging any gap of detection of any compound by either GCMS or LCMS.

It is already accepted in ISO 10993-18 and by FDA that metal elements are extracted predominantly in aqueous extracts, and their analysis is selectively analyzed by ICPMS. The same principle of selective analysis should apply to solvent extracts in which analytes are predominantly extracted. Polar solvents extract predominantly polar compounds, and LCMS is the selective instrument for analysis of this class of compounds. Non-polar solvents extract predominantly non-polar compounds, and GCMS is the selective instrument for analysis of this class of compounds. Semi-polar compounds are predominantly extracted in semi-polar solvents, and this class of compounds are analyzed by both GCMS and LCMS, bridging any gap of detection of any compound by either GCMS or LCMS.

Proponents of analysis of all extracts by all platforms may advocate the necessity of current practice under the pretext that the safety of the device is paramount; cost, resources and time should not be used to compromise the safety of the device.

However, experimental evidence and data review of reports show that compounds containing reactive functional groups, i.e., most toxic compounds, are either undetected or detected as reaction or degradation products. The degradation and formation of reaction products and complex species are enhanced by concentration, evaporation of solvent and reconstitution in a different solvent, a process routinely followed to meet the Analytical Evaluation Threshold (AET) or to make the extraction solvent amenable for injection. The time and resources spent to identify and quantify compounds in non-polar and polar extracts by LCMS and GCMS, respectively, do not result in detecting the most toxic extractables as observed in numerous reports. Therefore, it is recommended that the study design focus on identification of potential toxic extractables and performing targeted and selective analysis using appropriate analytical methods. This would improve the accuracy of the analytical data and ensure device safety.

The ISO committee should step forward and clarify the advantages of selective analysis with FDA. This would make the process more efficient and cost effective, saving valuable time and resources that are spent collecting insignificant, inaccurate, and insufficient data. This could eliminate current endless discussion amongst toxicologists, analysts, and every concerned stake holder to presumably satisfy FDA requirement. The most important criterion in chemical characterization is accuracy, and utilizing selective analysis of carefully selected solvents for extraction is the most efficient analytical approach.

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References:

1. Biological evaluation of medical devices: Chemical Characterization of medical device materials within a risk management processISO10993-18:2020(E).

2. Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" Guidance for Industry and Food and Drug Administration Staff. Document issued on: September 4, 2020.

3. M. Rahi and R. White. Effects of Analytical Evaluation Threshold (AET) on Quantification and Identification for Extractables and Leachables of Medical Devices: A Safety issue. MedTech Outlook. November Issue 2022.

4. Mourad Rahi and Mark Smith. Biocompatibility Failure & Solvent Effect on Chemical Characterization. Medical Device and Diagnostic Industry (MD&DI). Aug 05, 2021.

5. Mourad Rahi and Mark Smith. "Agonies and Thrills of Es and Ls. Part 2: Solvent Effects." SurFACTS in Biomaterials, Spring 2021, Volume 26.

6. Merck, LC-MS Contaminants. Common mass spectrometry contaminants and their sources. https://www.merckmillipore.com/INTERSHOP/web/WFS/Merck-HKSite/en_US/-/USD/ShowDocument-Pronet?id=201604.111.

7. Keller, Keller, B.O.; Sui, J.; Young, A.B.; Whittal, R.M. Interferences and contaminants encountered in modern mass spectrometry. Analytica Chimica Acta (Review/tutorial, Special Issue on Mass Spectrometry), 2008.

8. T. Stricker, R. Bonner, F. Lisacek, G. Hopfgartner. Adduct annotation in liquid chromatography/high-resolution mass spectrometry to enhance compound identification. Anal. Bioanal. Chem. (2020), 10.1007/s00216-020-03019-3.

9. Dwight Stoll. Contaminants Everywhere! Tips and Tricks for Reducing Background Signals When Using LC-MS. LCGC North America, LCGC North America-08-012018, Volume 36, Issue 8. Pages: 498-504.

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