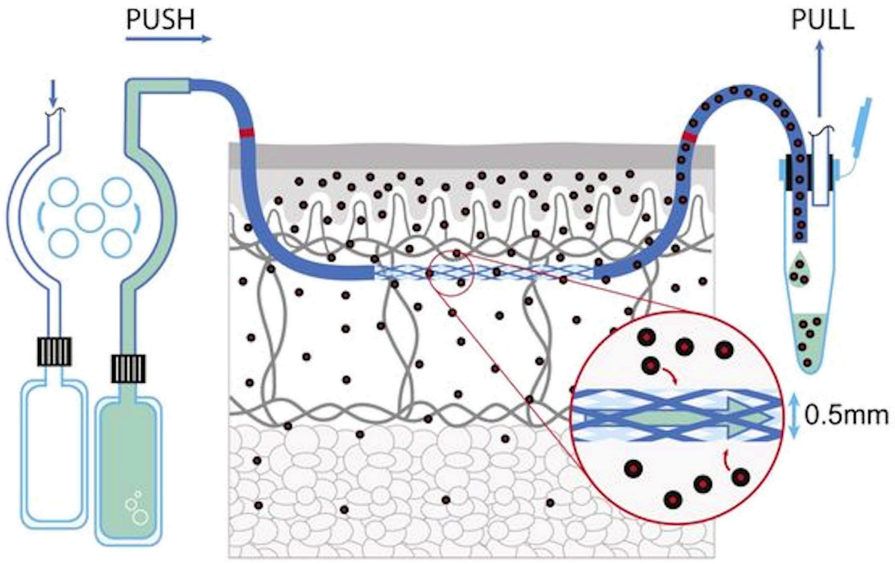
INTEGRATING DERMAL AND ADIPOSE OPEN FLOW MICROPERFUSION (dOFM & aOFM) IN PHARMACOLOGICAL & TOXICOLOGICAL STUDIES



Dermal and Adipose Open Flow Microperfusion (dOFM and aOFM) are cutting-edge techniques that enable continuous, real-time sampling of interstitial fluid (ISF) from skin and subcutaneous adipose tissue without disturbing the surrounding environment. These methods offer unparalleled insights into drug penetration, distribution, and metabolism in peripheral tissues, and enable the collection of data that traditional plasma sampling or tissue homogenization cannot provide.

BENEFITS OF dOFM AND aOFM SAMPLING:

1. ACCURATE ASSESSMENT OF LOCAL DRUG DISTRIBUTION:

- **Direct Measurement of Free, Unbound Drug Concentrations:** Unlike plasma sampling, dOFM and aOFM capture the pharmacologically active drug fraction within the interstitial space of skin and adipose tissue.
- **Transdermal Drug Evaluation:** Critical for assessing the bioavailability and penetration profiles of topically applied drugs, helping optimize formulations and dosing strategies.
- **Subcutaneous Drug Monitoring:** Essential for studying depot formulations, biologics, and gene therapies administered subcutaneously, enabling precise tracking of drug release and absorption.

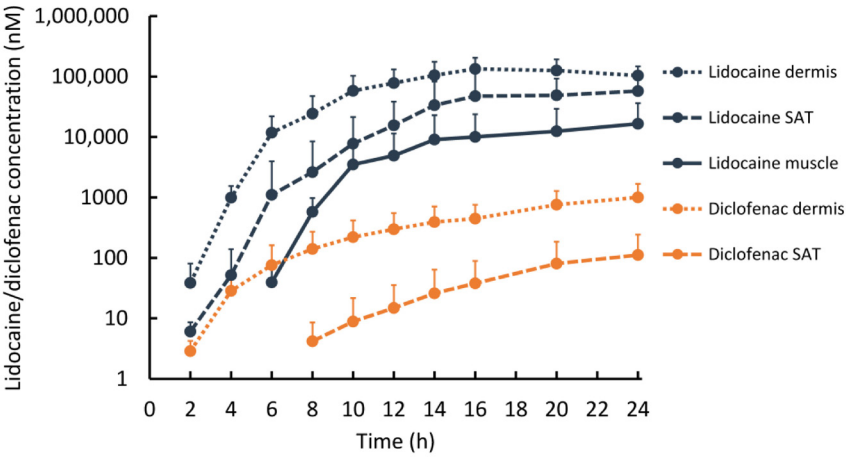
2. IMPROVED PHARMACOKINETIC AND PHARMACODYNAMIC MODELING:

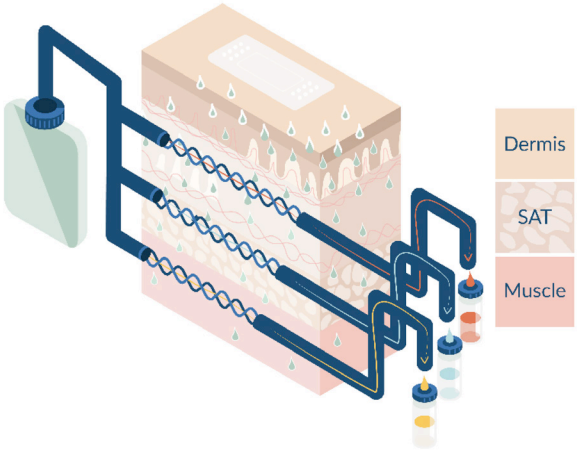
- **Real-Time Kinetics:** Continuous sampling provides detailed concentration-time curves, improving PK/PD modeling accuracy.
- **Longitudinal Sampling:** Serial sampling from the same animal reduces inter-animal variability and supports 3Rs principles.
- **Circadian Rhythm Considerations:** Enables monitoring of how drug distribution may fluctuate based on day/night cycles or metabolic activity in skin and fat tissues.

3. ENHANCED SAFETY PHARMACOLOGY AND TOXICOLOGY INSIGHTS:

- **Local Toxicity Monitoring:** Detects site-specific adverse effects, such as inflammation or necrosis, that plasma sampling may miss.
- **Inflammatory Biomarkers:** Measures cytokines, chemokines, and other markers of immune response in real-time, critical for assessing the safety of biologics and gene therapies.
- **Metabolic Profiling:** Reveals how drugs or their metabolites accumulate in peripheral tissues, identifying unexpected toxicological risks.
- **Smooth Transition to Clinical Evaluations:** Use the same OFM sampling methods in preclinical and clinical evaluations allowing for direct comparability of drug distribution and pharmacodynamics across species.

Multi-tissue evaluations are possible using OFM. In a recent study by Birngruber et al. (2023) OFM was used to sample the dermis, subcutaneous adipose tissue (SAT), and muscle in pig skin following application of lidocaine-containing adhesives and diclofenac topical gel to evaluate the ability of analgesic drugs to reach muscle tissue for treatment of musculoskeletal pain. In this study, OFM was successful in monitoring the drug penetration processes through the dermis, SAT, and muscle tissue. This provided a time-resolved concentration profile in each of the tissue layers.





Birngruber et al. (2023). Topical Delivery Systems Effectively Transport Analgesics to Areas of Localized Pain via Direct Diffusion. Pharmaceutics 15, 2563. https://doi.org/10.3390/pharmaceutics15112563

Dermal and adipose OFM have brought groundbreaking advancements to drug discovery and development, particularly for studying drug distribution and pharmacokinetics in the skin and adipose tissue, as well as surrounding tissue such as muscle. This tool gives researchers unprecedented insight into drug behavior at the site of action, supporting more precise dosing strategies, accelerating drug development timelines, and enhancing the prediction of clinical outcomes.

Visit https://www.basinc.com/open-flow-microperfusion-resources for a list of published references and other materials about the use of OFM for drug development.