42 | Enhanced access to the health-related skin metabolome by fast, reproducible and non-invasive WET PREP sampling

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The skin is our largest organ and influences our physical and mental health. Its chemical composition can reflect various environmental and disease conditions. The skin metabolome consists of all low molecular weight chemicals present on the skin, and by sampling the skin metabolome, we can provide a window into the mechanisms of body. However, the broad application of skin metabolomics has recently been hampered by a lack of easy, widely applicable, non-invasive sampling methods. The current standard, pre-wet swabs, is time intensive and significantly complicates clinical assays. Here, we present a novel rapid, simple, and most importantly, pain-less, non-invasive sampling technique suitable for clinical studies on fragile or weakened skin: WET- PREP. WET-PREP is simply a water lavage of the skin, which focuses on capturing the metabolome separately from the lipidome. We systematically evaluate WET PREPs in comparison with swab collection using LC-MS² on the two most commonly used separation modes in skin metabolomics: hydrophilic interaction chromatography (HILIC) and C18 reversed phase (RP). 22 healthy individuals were sampled at the left and right antecubital fossa using both sampling methods. Although both methods overlap in coverage, there are a high number of significantly different metabolites unique to the sampling method. WET PREP provides a strikingly more stable shared metabolome across sampled individuals, while also being able to capture unique individual metabolites with a high consistency in intra-individual reproducibility. Through cross-reference to the previous literature, the specific metabolites, which have potential relevance to skin function and health are more often isolated using WET-PREP. With the exception of (phospho-) lipidomics studies, we recommend WET-PREPs as the preferred skin metabolome sampling technique for clinical metabolomics due to the quick preparation time, low-cost, and gentleness for the patient. We also suggest, based on abundance and span across samples, L-Leucine and L-Proline as potential factors for normalization.