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Microfluidic Plasma Separation Integrated with SERS for label-free molecular Analysis of Blood Plasma

Blood plasma is widely used in clinical diagnostics owing to its rich molecular composition and reduced interference from cellular blood components. Conventional plasma isolation relies on centrifugation, which requires specialised equipment and limits deployment in decentralised and point-of-care settings. Here, we present an integrated microfluidic-SERS analytical platform for rapid label-free molecular analysis of blood plasma. The platform combines passive membrane-based plasma separation with downstream surface-enhanced Raman spectroscopy (SERS) and machine learning, enabling sample preparation and molecular analysis within a single workflow without centrifugation or external pumping. The device incorporates a polyethersulfone membrane within a multilayer polydimethylsiloxane architecture, enabling plasma extraction from whole blood under passive flow conditions without external pumping or centrifugation. The platform achieved a red blood cell removal efficiency of 98.9% with plasma recovery of $43.1 \pm 2.7\%$, within approximately 5 min. Analytical performance was evaluated using UV-Vis spectroscopy, Raman spectroscopy and Bland-Altman analysis, demonstrating strong agreement between LoC-derived and centrifuged plasma samples ($r=0.96$). These findings demonstrate that passive microfluidic plasma preparation can be successfully integrated with SERS while preserving analytical performance comparable to conventional centrifugation, supporting the development of rapid label-free sensing platforms for blood-based molecular analysis. Blood plasma is a critical biofluid for molecular analysis, but conventional separation methods such as centrifugation are time-consuming and require laboratory infrastructure, limiting their suitability for point-of-care applications. In this work, we present an integrated microfluidic SERS platform for rapid plasma separation and label-free molecular fingerprinting of blood samples. The device employs a membrane-based microfluidic design to isolate plasma from diluted whole blood under passive, capillary-driven flow conditions, achieving a red blood cell removal efficiency of $98.9\% \pm 1.3\%$ within five minutes with consistent performance across samples from multiple donors ($n = 6$). Separated plasma is analysed directly using commercially reproducible nanostructures gold SERS substrates, providing consistent signal enhancement with an average enhancement factor of $\sim 10^8$. Raman spectra obtained from microfluidic-separated plasma show a degree of agreement with those from conventionally centrifuged samples (Pearson coefficient $r = 0.96$), indicating preservation of the overall biochemical fingerprint. This study demonstrates a fully integrated microfluidic-SERS platform for plasma separation and molecular analysis without compromising analytical performance, with validated agreement to conventional centrifugation. The system provides a simplified sample-to-analysis workflow and represents a promising step toward compact, point-of-care molecular diagnostics. Future work will extend validation to larger and clinically diverse cohorts and evaluate performance using undiluted whole blood.