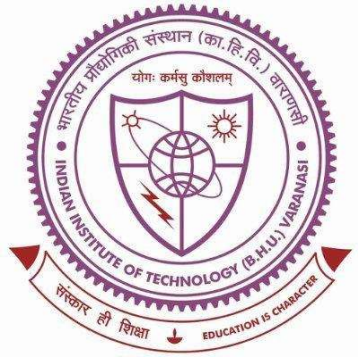
Development of Low-cost Portable Microfluidic Point-of-Care Devices for Estimation of Hematological and Biochemical Parameters



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By

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CHAPTER 6: CONCLUSIONS AND FUTURE WORK

This chapter summarizes the work presented in this thesis and also enumerates some important conclusions. It also provides a general direction that could be adopted to undertake further researches as a part of this dissertation.

6.1 Summary and conclusions

Summarily, this thesis provides some application of microfluidic devices especially paper-based devices and centrifugal devices, for the determination of pathological parameters such as hemoglobin, hematocrit, and creatinine using whole human blood.

Subsequently, the development of a low-cost reagent-free portable spinning disc for determining hemoglobin is described. This device can be implemented in under-served locations without sacrificing the fundamental principle of direct evaluation of hemoglobin extracted from human blood. The fundamental principle of osmotic hemolysis for hemoglobin extraction from red blood cells is explored. The method harnesses the dynamics of a blood droplet on a rotating platform and simple imaging to estimate hemoglobin within a turn-around time of around 13 minutes. These results are likely to pave the pathway of establishing the paradigm of a first-principle-based reagent-free evaluation of blood pathology in health and disease which can be considered as a paradigm shift in health care diagnostics without the application of any commercial reagent.

Subsequently, the development of a low-cost and simply-fabricated microfluidic paper-based analytical device (μPAD) to estimate plasma creatinine from the finger-pricked whole human blood is described. A simple paper strip is proposed to accurately measure creatinine concentration using just 10 μL of figure-pricked blood. The device involves three simple steps: plasma separation from whole blood, plasma transportation to

the detection zone, and quantifying the creatinine concentration using an in-house developed app. The predicted creatinine values are further benchmarked against the measurements from a biochemical auto-analyser.

Subsequently, a microfluidic paper-based analytical device (μPAD) has been developed to determine hematocrit and hemoglobin levels simultaneously. This device exploits the area of the stain formed by a spreading drop of 20 μL of whole blood on Whatman filter paper immobilized with sodium chloride and Ethylenediaminetetraacetic acid for hematocrit level, whereas for hemoglobin concentration, it utilizes the grey color intensity of a 20 μL droplet of a mixture of blood and deionized water. The performance of the device is further verified by comparing it with the gold-standard results of the automated hematology analyzer. This device is likely to provide a simple, fast, disposable, and inexpensive tool to determine the hematocrit and hemoglobin levels in resource-constraint settings.

Finally in the spinning disc platform, a simple, affordable, and portable blood test kit is developed for measuring plasma-creatinine concentration with 10 μL of whole human blood. This device exploits the centrifugal force for blood plasma separation inside a three-layer disc having channels in the form of a sector. In this method, the reaction between creatinine and alkaline picrate, known as the Jaffe reaction, is utilized to quantify the creatinine concentration based on the color intensity. Further, the values of creatinine measured with the present device are benchmarked against the gold standard results.

In the nutshell, this thesis envisioned the development of a multiplexed diagnostic blood test kit enabled by disruptive technology for better healthcare diagnostics at sufficiently low cost and establish the same through estimation of some hematological and biochemical parameters in low-cost portable devices combining the empowerment of

underserved population as human resources with the application of micro paper based analytical device and lab-on-a-compact disc.

6.2 Scope of future studies

Although the research demonstrated in this dissertation has made contribution to this dynamically evolving field, more efforts are still needed to improve the image analytics and device development.

1. In this dissertation, compact discs were fabricated using vinyl cutter and CNC machine. The top and bottom layer of the disc were engraved with CNC, and middle layer was machined with vinyl cutter. All three layers were then aligned manually and pressed to make a composite disc and passed through mechanical roller to make the device leakage-proof against the centrifugal force. This fabrication method is currently only suitable under laboratory conditions. For the purpose of the industrial-scale process and reduce the manual intervention, the microfluidic disc can be fabricated using other methods. For example, the disc can be fabricated with the help of 3D-printer which may reduce the manual intervention as well as layers for the composite device.
2. Here, we demonstrate the plasma extraction and colorimetric-based analyte detection in the same channel. There may be chances of interference of blood cells on the assay which leads to poor efficacy. Therefore, plasma can be extracted in separate chamber and can be distributed to the different chambers for the downstream analysis.
3. In this dissertation, colorimetric-based detection technique is employed for the measurement of analyte concentration with the help of the images captured by a smartphone. These devices are primarily meant to be used in field settings where imaging conditions greatly vary, resulting in less accurate results. Therefore, a light-box is used for image capturing which adds an additional accessories and light source.

To circumvent this, machine-learning (ML)-assisted models can be used for their ability to accurately predict analyte concentrations.