LAB-ON-A-DISC FOR SIMULTANEOUS ANALYSIS OF BLOOD CHEMISTRY AND IMMUNOASSAY

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ABSTRACT

We report a fully integrated lab-on-a-disc that can perform both of multiple chemical analyses and immunoassay on a disc. The concentrations of 12 analytes to test liver related diseases risk and Anti-HCV are reported within 30 minutes by simply inserting a disc to a portable device (Figure 1a). In our blood analyzer, whole blood is applied directly to a disposable disc containing 12 different kinds of reagents for the blood chemistry analysis as well as reagents required for the immunoassay to detect Anti-HCV. The absorbance can be measured at 10 different wavelengths to accommodate various kinds of reaction protocols.

KEYWORDS: Lab-on-a-Disc, Blood Chemistry, Immunoassay, Point-of-Care Device

INTRODUCTION

Lab-on-a-disc platform in which the centrifugal pumping is the physical principle to transfer liquid in microfluidic structures have garnered a great deal of attention because they could offer the advantages of miniaturization and automation for biochemical analysis. In order to control the fluidic passage, the majority of centrifugal microfluidic platforms utilized either hydrophobic valves or capillary valves. However, for the robust control of the valving operation, fine tuning of the spin speed as well as the local surface properties or dimension of the microchannels were required. Furthermore, these valves can function only as an opening valve; i.e. from normally closed state to open state, not the reverse. As a result, only a limited number of diagnostic tests that do not require complex fluidic design have been developed on a disc platform.

THEORY

We have demonstrated an innovative laser irradiated ferrowax microvalve (LIFM) that is based on phase transition of ferrowax, paraffin wax embedded with 10 nm sized iron oxide nanoparticles [1]. Laser light of relatively low intensity was able to melt the paraffin wax with embedded iron oxide nanoparticles, whereas a high intensity laser beam alone could not melt wax. This is because of the strong absorption of laser light by iron oxide nanoparticles. Using the innovative LIFM together with pathogen specific magnetic particles, we reported a fully integrated pathogen specific DNA extraction from whole blood on a portable lab-on-a-disc device [2]. We have demonstrated that our novel centrifugal microfluidic design enables a full integration of biological reactions that require complex batch mode microfluidic controls.

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EXPERIMENTAL

Figure 1b shows the microfluidic layout of the disc that can perform both of blood chemistry and immunoassay on the same disc. On the half of the disc, the total process of plasma separation and metering, mixing with dilution buffers and the distribution of diluted plasma to multiple cuvettes are fully automated for the blood chemistry analysis. On the other half of the disc, the total process of ELISA is fully integrated on the disc; 10 uL of serum is transferred to the mixer preloaded with microparticles coated with the HCV antigen. After incubation and washing out the serum residues, the addition of HRP conjugated secondary antibody, incubation and washing, reaction with TMB substrate are followed. Finally, the stopping solution is mixed and the final solution is transferred to the detection chamber before the absorbance is measured at 405 nm.

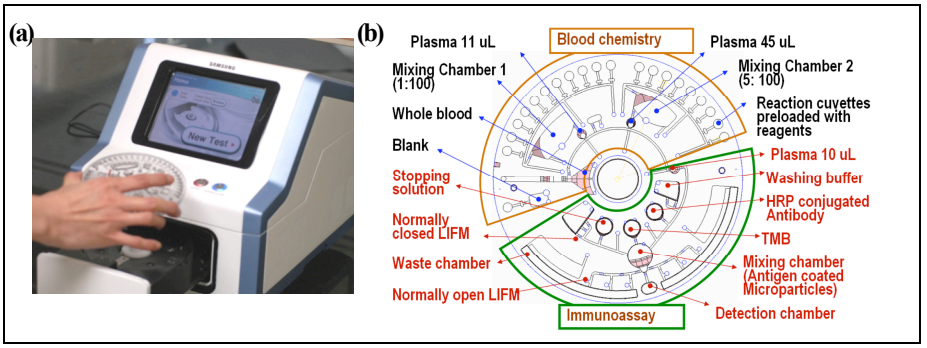

Figure 1. (a) A photo image of the SAIT blood analyzer and a disc containing dried reagents and dilution buffers (b) Disc design showing the detailed micro fluidic layout and functions.

RESULTS AND DISCUSSION

The concentrations of 12 analytes to test liver related diseases risk; ALB, ALP, ALT, AMY, AST, CHOL, DBIL, GGT, GLU, TBIL, TG, and TP are analyzed on the half of the disc. Five items including ALP, ALT, AMY, AST, and GGT are kinetic measurements; the analyte concentration is proportional to the slope of the absorbance change. Seven items including ALB, CHOL, D-BIL, GLU, T-BIL, TG and TP are end-point measurements; the saturated absorbance is proportional to the analyte concentration. In addition, six items including ALT, AST, T-BIL etc. require each 5 μL of plasma sample per 100 μL of reagent to have good sensitivity and dynamic range. However, six items including ALB, ALP, CHOL etc. each need 1 μL of plasma sample for best performance in dynamic range. As shown in Fig. 1b, the disc is designed to accommodate two different plasma dilution ratios. Examples of the performance of blood chemistry analysis are shown in Figure 2.

The half of the disc is used to measure the concentration of Anti-HCV. The basic concept of ELISA is directly used except that PS microparticles are used instead of PS plate to have large surface area. The spin program is optimized to run both of blood chemistry and immunoassay on the same disc. The total process from blood

injection to the detection of both 12 blood chemistry items and anti-HCV could be finished within 30 minutes

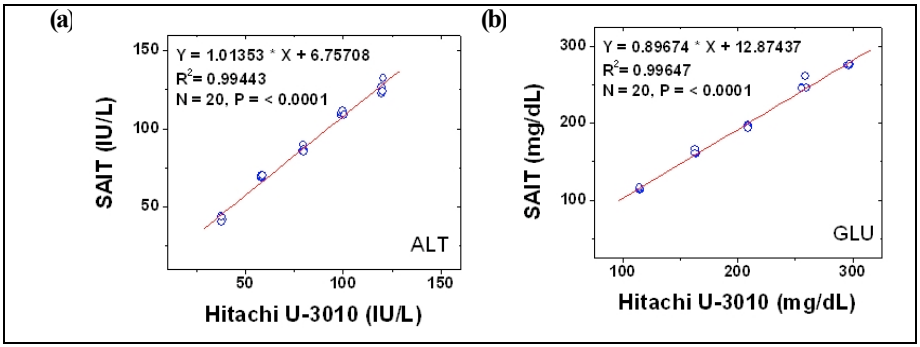

Figure 2. (a) Correlation of Alanine amino Transferase(ALT) concentrations measured at 340 nm by SAIT blood analyzer and Hitachi U-3010 (b) Correlation of glucose concentration measured at 500 nm by SAIT blood analyzer and Hitachi U-3010.

CONCLUSIONS

To the best of our knowledge, it is the first demonstration of the simultaneous analysis of a blood chemistry and antibody detection on a disc. In order to accommodate diverse reaction protocols and detection methods, the system is equipped with an optical detection unit that can perform colorimetric assays at 10 different wavelengths. Compared to the conventional blood analysis done in the clinical laboratories, the "Lab-on-a-Disc" is advantageous for the point-of-care applications because it requires less blood (200 μL vs 3 mL), takes less time (30 min vs several days), and does not require a specially trained operator or expensive instruments.

ACKNOWLEDGEMENTS

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