DESIGN AND ANALYSIS OF INTEGRATED PAPER BASED BIOCHIP WITH MICROHEATER FOR LAMP USING VIRAL MIMICKING NANO PARTICLES

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Thesis submitted in fulfillment of the requirements
for the award of the degree of
Master of Science

College of Engineering

UNIVERSITI MALAYSIA PAHANG

FEBRUARY 2022

ACKNOWLEDGEMENTS

First and foremost, I would like to express my gratitude to the Almighty for providing me with the courage, peace, health, and wisdom during this difficult time, as well as for guiding me in the right direction.

I thank my supervisor, Dr. Fahmi Samsuri, for his immense support, guidance, patience, and encouragement throughout my Master's journey with having high confidence in me. I am grateful to my co-supervisor, Dr. Vigneswaran Narayanamurthy, for his care, love, support, and ideas to conduct research as well as being a brother.

I want to express my gratitude to Dr. Sudhakaran, for treating me like a family member and for his many ideas and inspiration. Moreover, I would like to express my gratitude to Sreenath, Rajan, and Megaligam for their assistance and advice during my Master's programme.

I wish to thank Dr. Kumaran, for providing a thermal camera to carry out the research analysis. I would like to thank Dr. Hayder, Ms. Fiona, and the staff in CARIFF, UMP, for their support and training while using the microfluidics lab. I would also like to thank Ms. Puteri, IIUM, Kuantan for her assistance in fluorescent imaging.

I thank and acknowledge the financial support from UMP through UMP Internal research Grant (RDU1803183), Master Research Scheme (MRS), and UMP Post Graduate Research Grant Scheme (PGRS). Many thanks to the Institute of Postgraduate Studies (IPS) and Centre for International Relations (CIR) staff for their outstanding contributions.

Finally, I would like to express my gratitude to my parents (Mr. Ezhil Navaroji & Mrs. Sumetha), brother (Mr. Jyothish), relatives, and friends for their unwavering support during the ride. I also want to thank myself for believing in me, for having confidence in me, and for the thought of never giving up.

ABSTRAK

Virus ialah organisma berjangkit sub-mikroskopik yang menyebabkan penyakit kepada manusia, haiwan dan tumbuhan yang mengakibatkan morbiditi dan boleh menyebabkan kematian. Beberapa teknik, termasuk antibodi, antigen, dan RNA, boleh digunakan untuk mengenal pasti jangkitan virus. Walau bagaimanapun, modaliti pengesanan RNA dan antigen lebih disukai untuk mendiagnosis jangkitan aktif. Oleh itu, keperluan ujian titik penjagaan (POCT) dalam mengesan RNA dan antigen adalah luas, manakala teknik yang lebih sedikit tersedia disebabkan oleh keperluan struktur dan metodologi yang kompleks. Selain itu, penapisan sampel virus daripada darah adalah proses yang membosankan. Pengkomersilan cip berasaskan kertas dalam bidang penahanan pengesanan RNA disebabkan oleh penyelidikan tidak mencukupi dalam penyepaduan cip berasaskan kertas dengan teknik yang disesuaikan untuk pengesanan RNA virus. Memandangkan penguatan berlaku pada suhu tinggi, pemanas mikro tertentu digunakan, Tetapi pemanas mikro sama ada lebih mahal untuk digunakan semula atau murah untuk dilupuskan. Untuk aplikasi pakai buang berskala besar, teknik fabrikasi sputtering atau PVD memakan masa dan meningkatkan tenaga kerja. Penyepaduan cip kertas dengan pemanas mikro boleh guna semula untuk teknologi penguatan isoterma (LAMP) ubat gelung adalah penting untuk membangunkan diagnosis titik penjagaan (POC) mudah alih yang pantas dan mudah digunakan. Dengan mempertimbangkan semua kebimbangan ini, kami telah membangunkan cip kertas untuk penapisan berkesan zarah virus daripada sampel dan menyepadukannya dengan pemanas mikro boleh guna semula untuk menyediakan suhu yang diperlukan untuk memulakan ujian LAMP. Dalam penyelidikan ini, cip kertas aliran sisi dan menegak telah dibuat menggunakan pencetak laser dan pemotongan manual, dan kecekapan penapisan dianalisis menggunakan mikrosfera. Halangan hidrofobik dijana dengan mengapit cip kertas di antara polietilena tereftalat (PET) dan slaid kaca. Sifat berliang kertas penapis menapis zarah dalam sampel. Begitu juga, pemanas mikro berasaskan papan litar bercetak (PCB) telah direka menggunakan teknik goresan basah dan penganalisaan ciri terma. Keputusan cip kertas menunjukkan bahawa cip kertas aliran sisi tidak cekap disebabkan oleh pengkapsulan PET. Namun, cip kertas aliran menegak dengan salur masuk dan keluar gred 4 menapis 98.57% zarah yang tidak diperlukan daripada sampel dalam masa 5 saat. Selain itu, pembaziran cip boleh dikurangkan dengan menggunakan semula slaid kaca bawah dengan pensterilan yang betul. Analisis reka bentuk pemanas mikro mendedahkan bahawa konfigurasi meander mengatasi reka bentuk lain dengan perbezaan haba hanya ~8℃ dan penggunaan kuasa 1.79 W. Selain itu, lebar jalur pemanas mikro 1.75mm meningkatkan produktiviti. Di samping itu, pemanas mikro yang direka dengan penyebar haba mempunyai perbezaan terma hanya <5℃ jika dibandingkan dengan ~10℃ dalam pemanas mikro tanpa penyebar haba. Pemanas mikro yang dibangunkan adalah stabil selama lebih 6 bulan pada suhu bilik dan 10 hari di dalam air apabila dikapsulkan dengan PET. Akibatnya, ia mempunyai jangka hayat yang panjang dan boleh mengendalikan sampel biologi basah. Selain itu, pemanas mikro yang disepadukan dengan cip kertas berkesan memindahkan haba dengan perbezaan suhu 0.5 ℃. Oleh itu, pemanas mikro bersepadu cip kertas boleh membuka jalan untuk beberapa aplikasi seperti peranti makmal pada cip, ujian POC, ujian penguatan asid nukleik pantas, kultur sel dan penyelidikan biomolekul. Pada masa hadapan, biocip berasaskan kertas yang dibangunkan akan diuji untuk sampel biologi yang sebenar bagi mengesan jangkitan virus yang berbeza.

ABSTRACT

A virus is a sub-microscopic infectious organism that causes diseases to humans, animals, and plants resulting in morbidity and may cause mortality. Several techniques, including antibodies, antigens, and RNA, can be used to identify viral infections. However, RNA and antigen detection modalities are preferred to diagnose an active infection. Hence, the requirement of point-of-care tests (POCT) in detecting RNA and antigen is vast, whereas fewer techniques are available due to the requirement of complex structures and methodologies. Moreover, the filtration of viral samples from the blood is a tedious process. The commercialization of paper-based chips in the field of RNA detection holdups due to the inadequate research in the integration of paper-based chips with the techniques adapted for viral RNA detection. Since the amplification occurs at elevated temperatures, certain microheaters are employed, But the microheaters are either costlier for reuse or inexpensive for disposal. For large-scale disposable applications, sputtering or PVD fabrication techniques is time-consuming and increases the workforce. The integration of paper chips with the reusable microheater for loop-medicated isothermal amplification (LAMP) technology is crucial for developing rapid and easy-to-use hand-held point-of-care (POC) diagnosis. By considering all these concerns, we have developed a paper chip for effective filtration of viral particles from the sample and integrated it with a reusable microheater to provide the necessary temperature to initiate the LAMP assay. In this research, lateral and vertical flow paper chips were fabricated using a laser printer and manual cutting, and the filtration efficiency was analyzed using microspheres. The hydrophobic barriers are generated by sandwiching the paper chip between the polyethylene terephthalate (PET) and the glass slide. The porous nature of the filter paper filters the particles in the sample. Similarly, the printed circuit board (PCB) based microheater was fabricated using the wet etching technique and analyzed the thermal characteristics. The results of the paper chip convey that the lateral flow paper chip was inefficient due to PET encapsulation. Still, the vertical flow paper chip with grade 4 inlet and outlet filters 98.57% of unnecessary particles from the sample within 5 sec. Moreover, the wastage of chips can be reduced by reusing the bottom glass slide with proper sterilization. The design analysis of the microheater reveals that the meander configuration outperforms other designs with the thermal difference of only ~8°C and the power consumption of 1.79 W. Also, the microheater strip width of 1.75mm enhances productivity. In addition, the fabricated microheater with a heat spreader has a thermal difference of only <5°C when compared with ~10°C in a microheater without a heat spreader. The developed microheater was stable for over 6 months at room temperature and 10 days in water when encapsulated with PET. As a result, it has a long shelf life and can handle wet biological samples. Moreover, the microheater integrated with paper chip effectively transfers the heat with a temperature difference of 0.5°C. Thus paper chip integrated microheater can pave the way for several applications like lab-on-chip devices, POC assays, rapid nucleic acid amplification tests, cell cultures, and biomolecular research. In the future, the developed paper-based biochip will be tested for real-time biological samples to detect different viral infections.

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