Smartphone operable centrifugal system (SOCS) for on-site DNA extraction from foodborne bacterial pathogen

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ABSTRACT

The on-site recovery of nucleic acid from foodborne bacteria is in high demand to further understand on-site molecular diagnosis, which is especially applicable in developing countries. Here, we first proposed a smartphone operable centrifugal system (SOCS) for nucleic acid extraction with the assistance of a low power consumable motor and hydrogel beads. The SOCS consists of a centrifugal motor, 3D-printed cartridge, a nucleic acid collection column, and a smartphone. The SOCS shows excellent DNA extraction performance within 6 min, and it can operate more than 100 times using a smartphone. The purified effluent DNA was accumulated in the nucleic acid collection column. The performance of the SOCS was confirmed by amplifying the recovered DNA from *Escherichia coli* O157:H7. Moreover, the artificially inoculated food and blood samples also confirmed the performance of SOCS. The proposed SOCS provides an on-site operable nucleic acid separation platform in terms of simplicity, easy usability, cost-effectiveness, and portability in pathogenic point-of-care diagnostics.

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I. INTRODUCTION

On-site molecular diagnostics have become a game changer in the field of clinical applications, food safety, and forensic analysis by offering a rapid, simple, and accurate analysis.^{1–3} To date, most of the research has been focused on developing either a portable nucleic acid amplification system or an amplicon detection system with the assistance of a mobile phone.^{4–10} Although the performance of polymerase chain reaction (PCR) systems has dramatically improved, there has been difficulty in obtaining recovery of high-quality nucleic acids (NAs) from the biological and/or clinical samples for continuous upgradation of the performance and accuracy. State-of-the-art NA extraction techniques such as silica-based extraction, filter paper-based extraction, and phenol-chloroform-based extraction require improvement due to the use of toxic PCR inhibition chemicals, low extraction yield, complex operation steps, and necessity of trained personnel intervention.^{11–14} Moreover, the conventional NA extraction methods

have limitations regarding on-site applications due to bulky instrumentation, which limits equipment mobility necessary in the case of an outbreak of a pandemic/epidemic infectious pathogen (i.e., virus and bacteria).^{15,16}

To challenge the limitations of the current extraction methods, miniaturized NA extraction devices have been developed through either chemical or physical approaches.^{17–25} Yoon *et al.*²³ performed an RNA extraction on a lab-on-a-chip using pH-dependent reversible dimethyl adipimidate and applied the extracted RNA to the gene expression analysis. Gan *et al.* developed a filter disc-based DNA extraction microfluidic device by stacking a Fusion 5 filter, a polydimethylsiloxane (PDMS) membrane, as well as two PMMA layers that can extract DNA from human whole blood, dried bloodstains, saliva, and a cigarette butt sample in less than 8 min. Even though such tremendous developments have been recognized, most of the microdevices still involve expensive fabrication

processes, equipments, and labor intensive chip preparation procedures. Based on observations from the previous studies necessary improvements, an advanced DNA extraction method should be a compact, handheld unit for portable, low-power consumption, easy-to-use, disposable, inexpensive overall, and output adequate purified DNA by removal of the potential PCR inhibitory reagents to realize on-site genetic analysis.^{26–28}

To meet the requirements, we proposed a novel method of a smartphone operable centrifugal system (SOCS) for nucleic acid extraction from pathogenic bacteria by assisting with a hydrogel as a sieving matrix and a smartphone (or portable battery) as a power source for operating a centrifugal motor. We packed the porous hydrogel beads into a DNA separation cartridge to isolate NAs from cell debris by applying a centrifugal force using a mobile phone-powered motor. To evaluate the performance of the SOCS, we conducted real-time PCR using purified DNAs from *Escherichia coli* O157:H7 (*E. coli* O157:H7) by SOCS. Successful application to the downstream analysis demonstrates that our SOCS has capabilities for the on-site DNA extraction with simple operation, rapid and high-quality DNA recovery, low power consumption, and portability.

II. EXPERIMENTAL

A. Concept of SOCS

The concept of SOCS is illustrated in Fig. 1(a). The SOCS is easily achievable by the modification of a flexible and portable power source (mobile phone or portable battery) and a universal serial bus

(USB) mini cooling fan. After purchasing the cooling fan, we modified the fan for connection to a pair of 3D-printed cartridge holders. The separation cartridge consists of a nucleic acid collection column and a lysate loading column with a plastic support, which contains a 5 mm-diameter nylon mesh filter and Sepharose 2B hydrogel beads (Sigma-Aldrich, USA) as shown in Fig. 1(b). Sepharose 2B hydrogel beads are utilized for size-based separation of NAs from the cell lysate using its pore size. A real photo image of the separation cartridge is shown in Fig. 1(c), in which the nylon mesh filter (dye in red) and the Sepharose 2B hydrogel beads (dye in green) were packed in the lysate loading column. A digital image of SOCS equipped with a mobile phone is displayed in Fig. 1(d).

B. Fabrication of the SOCS

The mobile phone-powered handheld nucleic acid extraction system was made by modifying a mini handheld fan [Fig. 1(a)]. Two metal connection hooks are fixed on the motor head in 180° direction and two 3D-printed cartridge holders are linked to the metal hooks which carry a separation cartridge in the each of the holders. Prior to loading the porous hydrogel beads into the lysate loading column, a 3-mm diameter of nylon mesh membrane was inserted inside the lysate loading column to prevent loss of the hydrogel beads during the separation [Fig. 1(b)]. After loading 1 ml of the hydrogel beads, the lysate loading column was put into the nucleic acid collection column. In order to prevent potential leakage and collapse during the rotation, the two columns are carefully aligned and its weight is balanced.

FIG. 1. (a) A structure of a SOCS that consists of a motor with two connection hooks, a pair of 3D-printed cartridge holder with two separation cartridges, and a USB connector. (b) Exploded view of the separation cartridge including a lysate loading column with a 5 mm-diameter nylon mesh and Sepharose 2B hydrogel beads, and a nucleic acid collection column. (c) Digital image of the lysate loading column (left) containing the Sepharose 2B hydrogel beads (dye in green) and the nylon mesh (dye in red) as well as the nucleic acid collection column (right). (d) Photograph of the SOCS connecting with a smartphone.

C. DNA extraction using SOCS

A DNA extraction was carried out using SOCS by applying a centrifugal force. A schematic image of the DNA extraction procedure is displayed by comparing with a silica-based commercial DNA extraction kit in Fig. 2. Pathogenic bacteria were thermally lysed at 95 °C for 5 min in 100 μ L distilled H₂O and then the lysate was loaded into the separation cartridge. One pair of the separation cartridge (53 $\times$ 15 $\times$ 8 mm³) fits into the 3D-printed cartridge holders which were hung on the connection hooks. To isolate the DNA from the lysate, 500 rpm centrifugal force was applied by plugging in the USB connector to a mobile phone for 1 min at room temperature (25 °C). The eluted DNA solution was recovered at the nucleic acid collection column.

D. Confirmation of DNA extraction performance of the SOCS

E. coli O157:H7 (ATCC 9637) was chosen as a model pathogen to confirm the DNA extraction using the SOCS. *E. coli* O157:H7 which was cultured using LB broth at 37 °C for 18 h. Cultured *E. coli* O157:H7 were 10-fold serially diluted from 10⁸ to 10³ and the prepared cells were used for downstream DNA extraction. A G-spin Genomic DNA Extraction kit (Cat No. 17121, iNtRON, Republic of Korea) was served as a DNA extraction reagent for

recovering the DNA from the cultured *E. coli* O157:H7 as a control experiment. SpeedSTAR™ HS DNA Polymerase was used for performing a real-time PCR using an *stx2* gene targeted TaqMan probe (5'-FAM-CTA TCA GGC GCG TTT TGA CCA TCT TCG-TAMRA-3') with a forward primer (5'-GGG CAG TTA TTT TGC TGT GGA-3') and a reverse primer (5'-TGT TGC CGT ATT AAC GAA CCC-3') on the mic Real-Time PCR system (Bio Molecular Systems, Australia).²⁹ Total 25 μ L Real-Time PCR reagent consisted of 2.5 μ L 10 $\times$ fast buffer I, 2.5 μ L Speed STAR DNA Polymerase, 3.0 μ L dNTPs (TaKaRa), 2 μ L primers (0.15 μ M) and Taqman probe (0.065 μ M), 1 μ L extracted DNA, and water to a final volume of 25 μ L. The thermal cycling temperature for real-time PCR was adjusted as follows: initial denaturation at 95 °C for 5 min followed by 40 cycles of 95 °C for 5 s, 60 °C for 15 s, 72 °C for 10 s, and a final extension step at 72 °C for 3 min.³⁰ For extracting genomic DNAs from food and clinical samples, we tested artificially infected milk, pork, and human blood. *E. coli* O157:H7 (10⁵, 10⁴, and 10³ cells) was spiked into the milk, pork, and human blood samples and was thermally lysed at 95 °C for 5 min. The milk was obtained from Seoulmilk (Seoul, Korea). The pork was purchased from Nonghyup Agribusiness Group Inc. (Seoul, Korea). The blood (IPLA-WB1) was from Innovative research (MI, USA). After the DNA separation using the SOCS, the recovered DNA at the nucleic acid collection column was used for real-time PCR.

FIG. 2. Operation procedure of the SOCS in comparison with a commercial DNA extraction kit. The SOCS recovers pure DNA solution within 6 min by simply loading a thermally lysed *E. coli* O157:H7 into the separation column and applied a centrifugal force while the commercial kit takes more than 30 min with complex operation steps.

This study was approved by the Institutional Review Board (IRB, IRB-18-240) at Korea Advanced Institute of Science and Technology.

III. RESULTS AND DISCUSSION

A. Fabrication and operation processes of SOCS

The principle of the proposed device and system is schematically illustrated in Fig. 1. The designed SOCS uses centrifugal force to extract DNA from the bacteria cell lysate in a simple column-type tube combined with a modified handheld fan, which is able to supply an external centrifugal force by connecting to a mobile phone. Based on the stable electrical output performance of currently used mobile apparatus in a wide range of circumstances, the proposed gene extraction principle can be generally applicable to various mobile devices including smartphones or portable batteries. Considering this, we selected the smartphone when considering portability and usability in terms of a power source. The SOCS consists of three main parts containing the mobile phone-connected fan, the 3D-printed cartridge holder, and the separation cartridge as shown in Fig. 1(a). The portable fan contains the USB connector and motor, and the modified fan with a connection hook can hold the 3D-printed tube holder. To separate the DNA from the cell debris by using the separation cartridge, a reticular structure polymer called Sepharose 2B was packed on the nylon mesh filter based on the size exclusive chromatographic analysis. The separation cartridge consists of a lysate loading column and a nucleic acid collection column [Fig. 1(b)]. Figure 1(c) shows the manipulated separation cartridge component, and the lysate loading column designed in relatively small size to be properly inserted into the nucleic acid collection column, enabling the extracted DNA to be purely concentrated in the bottom of the nucleic acid collection column. Considering the common power supply module of the fan, a smartphone could stably provide the electricity to the developed SOCS as shown in Fig. 1(d). The rpm of the SOCS cartridge was measured by a tachometer (DT-2234B) to verify the centrifugal force. As a result, the rpm was determined as 500 rpm which correspond to 15 g-forces. Considering the conventional centrifuge system, the SOCS cartridge rpm powered by a mobile phone is sufficient to apply for the DNA extraction.

The developed SOCS system significantly reduces the DNA purification time and apparatus size in comparison with commercial DNA extraction methods, which involve a bench-top size centrifuge (Fig. 2).^{31,32} To extract bacterial DNA from the cell lysate, the prepared cells are lysed by incubating the bacterial cells in a 95 °C thermal block for 5 min, and the cell lysate was loaded to the top of the Sepharose gel. Subsequently, the cell debris-loaded cartridge installed on the 3D-printed holder with the rotator. Although a plural holder pairing could be available, the volume balance must be adjusted, thus the SOCS can perform DNA extraction on two columns at the single operation. The lysate loading column was finally removed and the bacterial DNA obtained from the nucleic acid collection column. Extracted DNA was transferred for DNA amplification and analysis using real-time PCR. Unlike the current commercial DNA extraction method, which required a laboratory scale centrifuge with a relatively complicated method for the 30 min, the developed SOCS system could obtain pure DNA

within 6 min without any expensive equipment nor experts to operate it (Movies S1 and S2 in the [supplementary material](#)). Additionally, it is operable via portable batteries or smartphone with low power consumption. The employed portable fan operates at DC 3–5 V with 1 W of power consumption. Regarding the 3000 mAh of the battery capacity of a common smartphone, the portable fan could continuously work for 12 h which is equivalent to 144 times of DNA extraction. The centrifugal system only costs about \$2 and easily obtained from the market without any difficulties. Therefore, the developed SOCS-based DNA extraction principle is suitable for POCT due to its simplicity, cost-effectiveness, low-cost, high portability, and easy operability.

B. Nucleic acid extraction using SOCS

Silica-based solid phase extraction column in the presence of chaotropic salt is the most commonly applied DNA extraction method which requires a high amount of input DNA and elution buffer.^{33,34} In fact, the total amount of DNA from the clinical sample for the on-site detection uses small volume (less than 1 μ l) of the pure DNA. Because of the small volume consumption, highly concentrated DNA in a small volume requires sensitive detection of the target pathogen. The SOCS is able to recover pure

FIG. 3. (a) Results of the slab gel electrophoresis for the PCR product amplified using DNA recovered from the SOCS and commercial kit. (b) Real-time PCR result curve from an extracted DNA using the SOCS with different volumes (10 μ L: red line and 100 μ L: blue line) of the elution buffer and a commercial kit (black). No Ct value was detected with the negative control (green line).

DNA using a relatively small amount of elution buffer with high DNA concentration. To demonstrate the feasibility of the SOCS, PCR amplification was carried out using the extracted DNA from the proposed system with a comparison of a commercialized kit. Bacteria cell (cell number: 10^8) in the different volume ($10\mu\text{l}$ and $100\mu\text{l}$) was loaded into the lysate loading column for DNA separation from cell debris and the recovered DNA was applied to the PCR amplification. Figure 3(a) shows resulting images from the gel electrophoresis via PCR products. The positive signals could be clearly obtained from PCR products using a recovered DNA from the commercial kit and SOCS with $10\mu\text{l}$ and $100\mu\text{l}$ elution solution while no signal was confirmed from the negative control. PCR amplicon with 120 bp was constantly observed in the positive control as intended that demonstrates the feasibility of designed SOCS-based DNA extraction principle. In this experiment, we were able to find the DNA purification ability of the SOCS for the downstream PCR application. However, the results could not explain our hypothesis, that a small volume of elution buffer would improve the detection signal of the PCR, due to the difficulty of relative quantification of PCR product using electrophoresis.

To prove our hypothesis, the eluted DNA solution was employed to perform a real-time PCR experiment and the resultant graph is shown in Fig. 3(b). The Ct value from the DNA solution recovered from $100\mu\text{l}$ was 20.03 which marked similar Ct value

(20.02) with the commercial kit. As we expected, the Ct value (18.36) from the DNA extracted from $10\mu\text{l}$ is lower than the commercial kit and DNA from $100\mu\text{l}$ lysate due to the highly concentrated DNA solution in a small volume. This feature enables to improve the Ct value of real-time PCR which making SOCS easy to apply for the on-site applications.

C. Performance evaluation of the SOCS using a real sample

To evaluate the DNA extraction capability of the SOCS, a different amount of bacteria cell numbers were thermally lysed and was inserted into the separation cartridge. The DNA purification and concentration was successfully accomplished by simply rotating the motor, which was powered using a smartphone. Figure 4(a) shows the real-time PCR results of DNA recovered from bacteria lysate solution using the SOCS and the conventional kit. The Ct values of real-time PCR from SOCS were 23.18, 28.91, 31.51, 36.04, and 40.41, while the Ct values from the extracted DNA using commercial kit were 25.42, 29.57, 33.96, 38.10, and 41.72 with 10^7 , 10^6 , 10^5 , 10^4 , and 10^3 *E. coli* O157:H7 cells, respectively. These results demonstrate that our DNA extraction method has better performance for real-time PCR with overall cell numbers in comparison with the commercial kit. In particular, lysate from 10^3 *E. coli* O157:

FIG. 4. (a) Ct values of the real-time PCR from the extracted DNA using the SOCS and commercial kit with different *E. coli* O157:H7 cell numbers. (b) Schematic image of the DNA extraction process from an artificially infected blood and food samples. (c) Ct values from real-time PCR with a pathogenic DNA that was extracted from an artificially infected milk, blood, and pork sample.

H7 were high enough to be able to extract and concentrate the DNA which probes efficient DNA recovery capability of the SOCS. The total operation time was 6 min including cell lysis, DNA separation, and recovery. Thus, our extraction system would be adequate for on-site, rapid, and sensitive pathogen identification which can be incorporated as a portable genetic analysis system.

Furthermore, DNA purification/concentration from artificially infected food and blood samples were conducted with the SOCS. Figure 4(b) schematically illustrates the detailed processes for the extraction of DNA from the infected samples. After the lysate was loaded into the separation cartridge, the continuously applied centrifugal forces to the SOCS enabled separation of DNA from the cell debris and food mixture. The obtained filtrated DNA products were further analyzed using real-time PCR. In particular, the performance validation of the SOCS was also investigated with artificial infected human blood, milk, and pork by pathogenic bacteria. After lysis of the real samples, the mixture was simply loaded into the tube and centrifuged DNA at 500 rpm. Interestingly, all the solid particles including cell membrane and food fragments remained at the lysate loading column and the DNA easily collectible from the nucleic acid collection column. To confirm the effectiveness of the SOCS, the separated product was carefully examined by genetic analysis using real-time PCR by the target *stx2* gene. The real-time PCR results using recovered DNA from 10^5 to 10^3 CFU/ml *E. coli* O157:H7 revealed that the Ct values from the extracted DNA were successfully recovered from the artificially infected *E. coli* O157:H7 in milk, blood, and pork meat [Fig. 4(c)]. Although the pathogens are mixed under different conditions such as viscosity, density, and various particle size, the obtained Ct values exhibited similar Ct values from the same number of the inserted pathogens. These results support the effectiveness of DNA extraction performance of the SOCS.

IV. CONCLUSIONS

In this work, we reported the method (SOCS) for the on-site nucleic acid extraction from pathogenic bacteria with the assistance of a low power consumable motor and hydrogel beads. The lightweight (40 g) and the easy-carriable motor is supplied an electric power using either a smartphone or portable batteries. Additionally, the repeated DNA extractions were successfully performed with a smartphone (battery size of 3000 mA) at least 140 times. We demonstrate its performance by amplifying the gDNA of *E. coli* O157:H7 using real-time PCR which shows better performance for the sensitive target bacteria identification comparing with commercial kits. Furthermore, pathogenic DNA was recovered from the artificially infected blood and food samples which indicate that our SOCS provides an adequate methodology to apply for the clinical diagnosis. Based on the obtained results, our findings strongly support that the SOCS enables us to use as on-site NA separation tools for point-of-care analysis.

SUPPLEMENTARY MATERIAL

See the [supplementary material](#) for checking out the SOCS operation for DNA recovery with a mobile phone and a portable battery (movie 1 and movie 2).

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