One-Touch-Activated Blood Multidiagnostic System using a Minimally Invasive Hollow Microneedle Integrated with a Paper-Based Sensor

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Supplementary Information

Fabrication of the biocompatible hollow microneedle: Negative photoresist SU-8 2050 (MicroChem Corp., Westborough, MA., USA) was spin-coated onto a 120 μm-thick flat glass panel. After placing on a 120 °C hot plate for 5 min and cooling 10 to 60 °C, the pillar with a diameter of 300 μm was used to draw the SU-8 at a rate of 10 μm s⁻¹, producing a microstructure with a height of 3,600 μm. This SU-8 mold was cured for 30 min at room temperature to solidify the polymeric bridge, and then separated from the frame at a drawing speed of 700 μm s⁻¹. A SU-8 solid microneedle (MN) was fabricated with a height of 1,800 μm and tip-diameter of 60 μm. After a silver layer was deposited onto the surface of the solid microneedle by Tollen’s test, nickel electroplating was performed to fabricate a nickel microneedle with a wall thickness of 30 μm. The 15° bevel angle was induced at the tip of the nickel microneedle by laser cutting (K2 Laser System, Inc, Gyeonggi-Do, Korea), and then the solid mold was removed by SU-8 Remover (MicroChem Corp.) to complete the hollow microneedle. Finally, a 1 μm-thick parylene film was thermally deposited on the surface of the microneedle by a parylene coating system (Femto Science Inc., Gyeonggi-Do, Korea). All parylene coating processes were performed under vacuum conditions in 1.5 h, and the parylene film thickness was controlled by setting a quartz crystal microbalance in the deposition chamber.

Fig. S1 Schematic diagram of the fabrication process of biocompatible hollow microneedle (MN). i) a three-dimensional SU-8 solid mold was obtained by a drawing lithography method; ii) nickel was electroplated onto an SU-8 solid mold; iii) a bevel angle was introduced and the solid SU-8 mold was removed; iv) a biocompatible parylene film was coated onto the inner and outer surface of the hollow microneedle.
Fabrication of the patterned nitrocellulose (NC) membrane: The Y-shape NC membrane pattern was fabricated by “tear-off patterning”. Briefly, the Y-shape pattern was designed by Silhouette Studio software (version 3.3.451), and the paper template was fabricated using a craft cutter. After, treatment of the paper template with dimethyl sulfoxide (DMSO) was conducted by pipetting, and the NC membrane and the template were placed on a glass support facing each other. After 25 min, the template and membrane were incubated in a dry oven heated to 37 °C, for 15 min. Finally, the stamped area was removed with forceps.

Fig. S2 Schematic of the fabrication process of Y-shaped nitrocellulose (NC) membrane by the tear-off patterning method. i) Paper template fabrication by craft cutter; ii) solvent treatment on template; iii) stamping the solvent treated template to the NC membrane; iv) drying, and v) tearing off the stamping region.
**Figure S3**

![Schematic diagrams and photograph images for optimization of sensor structure.](image)

**Fig. S3** Schematic diagrams and photograph images for optimization of sensor structure. The paper-based sensor contained (a and d) only sample pad (fusion 5 8151-6621); (b, c, e, and f) sample pad and asymmetric polysulfone membrane; and (c and f) nitrocellulose membrane treated with 0.5% surfactant 10G.

**Supplementary Table S1. In vitro whole-blood sample analysis**

<table>
<thead>
<tr>
<th>Rabbit #</th>
<th>Glucose concentration (mg dL(^{-1}))</th>
<th>Cholesterol concentration (mg dL(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lab Analyzer</td>
<td>OBMS</td>
</tr>
<tr>
<td># 1</td>
<td>138</td>
<td>145.5 ± 2.43</td>
</tr>
<tr>
<td># 2</td>
<td>153</td>
<td>153.9 ± 6.54</td>
</tr>
<tr>
<td># 3</td>
<td>128</td>
<td>137.8 ± 4.87</td>
</tr>
</tbody>
</table>

Comparison of the one-touch-activated blood multidiagnostic system (OBMS) and lab scale analyzer (Lab Analyzer; FUJI DRI-CHEM 4000 Chemistry Analyzer). Values are expressed as mean ± SD (n = 3).

**Supporting Videos:**

15 Supplementary Video 1: *In vitro* one-touch-activated blood diagnosis (Video clip: 2.36 MB)

Supplementary Video 2: *In vivo* one-touch-activated blood diagnosis (Video clip: 6.95 MB)