BLOOD PLASMA SEPARATOR USING MICRO PILLARS ARRANGED LIKE A LABYRINTH
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ABSTRACT
The goal of this research is to realize a blood plasma separator from whole blood, which enables to be fabricated in a healthcare devise using MEMS technology. This plasma separator has a unique and original idea that many micro pillars are arranged like a labyrinth. When whole blood is injected only by the driving force of capillary action, red blood cells are captured sequentially by a labyrinth which prevents from clogging up. Finally red blood cells are captured over the whole area of the blood plasma separator, and as a result blood plasma is extracted outside. We report a concept of this blood plasma separator, fabrication method and experimental results.

KEY WORDS: Blood Cell, Blood Plasma, Separator, Micro Pillar

INTRODUCTION
Many kinds of blood plasma separator have been developed to be fabricated into micro devices. Almost all separators have narrow gaps, weirs or micro pillars in micro capillaries to prevent blood cells from passing through. Because micro capillaries become clogged with blood cells easily, cross flow-type separators have been experimented with and reported; in those, the directions of the flow of whole blood and the flow of blood cells intersect with each other [1-4]. However, they were not efficient enough. This paper reports a new blood plasma separator that enables separation and collection of blood plasma efficiently.

We have proposed a blood plasma separator in which many micro pillars are arranged to form many pockets over the blood plasma separator area like a labyrinth [5]. When whole blood enters the blood plasma separator, blood cells are captured in pockets sequentially in the whole area of the blood plasma separator, and blood plasma passes through gaps between the pillars of pockets and then exits the blood plasma separator. Because of the flexibility of the red blood cell, the gap width was very important to obtain the performance of speed and efficiency. We report on these difficulties.

METHOD
Figure 1 shows a schematic diagram of the blood plasma separator that has many micro pillars arranged to form many pockets over all separation area like a labyrinth. When whole blood is injected from the left side and flows by capillary action, red blood cells are captured by pockets; on the other hand, blood plasma passes through gaps of these micro pillars. By distributing these micro pillars over the area of the blood plasma separator, red blood cells will be captured gradually from the front side of the separator and blood plasma will pass through the gaps of micro pillars. Finally, red blood cells will be trapped over the entire surface of the blood plasma separator, and blood plasma will be extracted in a forward direction. Figure 2 shows size and location of micro pillars. The micro pillars were 3.44×3.44 μm² or 3.44×2.58 μm² at the base, and 5 μm in height, the gap width of each micro pillars was 1.72 μm. We had reported the result obtained when the gap width of each micro pillars was 0.86 μm [5] and it took long time to finish the separation. In this report, the gap was extended from 0.86 μm to 1.72 μm to fasten the separation.

The blood plasma separator was fabricated by using photolithography. Figure 3 shows the dimension of the blood plasma separator. The device was consisted of inlet, fluid path, blood plasma separator area, plasma extraction path and outlet. Two photo-masks were used to fabricate the blood plasma separator device; one was for the fluid path and another for micro pillars of the
blood plasma separator area. These photo masks were prepared on the glass substrates by using Micro Stereo-lithography System ACCULAS and vapor deposition process.

Figure 3. Dimension of the plasma separator: (a) shows the plasma separator and (b) shows the fluid path from inlet to front of plasma separation area.

Figure 4. Photograph of a Plasma Separator and micro pillars. Filter area is 510×510μm², each micro pillar is 5μm in height.

It is very difficult to fabricate micro pillars on a glass substrate accurately and stably, we proposed an idea that the micro pillars were fabricated on the photo mask substrate for the micro pillars. The fabrication process had two steps. First step was that the photo resist was coated on a photo mask for blood plasma separator having micro pillars and exposed with conventional UV radiation from the back side of the photo mask substrate. Second step was that the resist coated photo mask was aligned with the photo mask for fluid path and exposed again with conventional UV radiation from the side of the photo mask for fluid path. After the developing process, the structure of the blood plasma separator and the fluid path was obtained.

Figure 3 shows the dimension of the blood plasma separator and the fluid path. (a) shows the plasma separator and (b) shows the fluid path from inlet to front of the plasma separation area. The cross section of the fluid path is 510μm in width and 5μm in depth. The depth of the fluid path is very narrow and it was very difficult to cover the fluid path by using plastic cover. To conquer this difficulty, lozenge shaped pillars were fabricated at the middle of the fluid path.

Figure 4 shows the photographs of a plasma separator and micro pillars. a) shows a whole view of the blood plasma separator. b) and c) show micro structures. These photographs were measured by using laser scanning confocal microscopy. Micro pillars were fabricated by photolithography using photo resist SU-8 3005. The micro pillars were 3.4×3.4 μm² or 3.44×2.58 μm² at the base and 5 μm in height. The gap width of each micro pillars was 1.72 μm and the entire area of the blood plasma separator was 510×510 μm². The micro plasma separator had the edge structure which prevent from passing blood cells threw the blood plasma separator. The substrate was finally covered with PET plastic sheet of 50μm thickness.

EXPERIMENTAL RESULTS

Figure 5 shows experimental results obtained by using human whole blood. a) to c) shows series of the experimental results taken in time series. a) shows the moment when whole blood reached the front edge of the blood plasma separator. b) and c) show the moments when the whole blood was separated into blood cells and blood plasma. The dark red area in these pictures shows red blood cells captured by pockets surrounded by micro pillars. The glowing light yellow zone shows separated blood plasma. d) shows blood plasma extracted from the end of the blood plasma separator area. Finally, blood cells were captured over the whole area of the blood plasma separator and blood plasma was extracted.

Figure 6 shows the enlarged photograph of the blood plasma separator filled with red blood cells. The photograph shows that a lot of blood cells were captured and filled by many pockets over the whole area. Blood cells were very flexible, became circle in wide space and changed the shape in narrow space. The driving force was only capillary action and the reveal of capillary action was controlled by using the plasma reactor. When plasma treatment was weak, capillary action was also weak and it took very long time to finish the plasma separation. On the other hand, plasma separation rate or efficiency was superior. When plasma treatment was strong, capillary action was also strong and it took very short time to finish the plasma separation. But plasma separation rate or efficiency was inferior. The plasma treatment and the gap width of pillars were the important parameters to obtain optimum plasma separation speed. In this experiment, a few minutes were necessary to obtain optimum plasma separation.
Figure 7 shows the enlarged photograph of the blood plasma separator taken in time series. Photographs (1) – (4) show that the blood cells were captured by the pockets gradually.

CONCLUSION

A blood plasma separator that is able to be fabricated into a micro device was designed and experimented with. It was demonstrated that micro pillars arranged like a labyrinth, captured red blood cells successfully and separated blood plasma. Because this plasma separator does not have to be added pressure from outside, there is no destruction of the blood cells. In the experimental result, whole blood penetrated in a filter and blood cells were captured and almost plasma was extracted by front course. The plasma treatment and the gap width of pillars were the important parameters to obtain optimum plasma separation speed. In this experiment, a few minutes were necessary to obtain optimum plasma separation.

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REFERENCE


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