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A novel hand-held viscometer applicable for point-of-care

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ABSTRACT

A novel hand-held viscometer was developed, which may be applied for measuring blood viscosity in point-of-care (POC) environment. Measurement process can be completed automatically in a single step within a few minutes using only 40 μL of a sample fluid. In spite of the importance of measuring blood viscosity, practical and widespread use of a viscometer as a medical device has been deterred mainly due to limitations of requiring large amount of blood sample and multiple steps for measuring process. Single-step automatic process with small sample volume was made possible by installing a metal sphere (0.8 mm in diameter) inside a capillary tube (1.05 mm in diameter) using bovine serum albumin (BSA) as a "bio-glue". Falling time of the metal sphere through a sample fluid in the capillary tube was measured by reading travel distance of 30 mm by the sphere. Qualitative and quantitative test to examine performance of the "capillary falling ball viscometer (CFV)" were carried out using aqueous solutions of triethylene glycol (TEG) and diethylene glycol (DEG). We used TEG and DEG instead of blood since wide range of viscosities can be easily prepared simply by mixing the glycols with water. In the qualitative experiment, fairly consistent falling times were produced for various concentrations of the TEG under different measuring angles (10°, 20°, 30°, 45° and 90°). The quantitative performance of CFV was analyzed using DEG solutions at 20° angle, resulting reasonable consistency when compared with publicized viscosity values. Also blood samples from patient and healthy people were used to measure viscosity under different angles, producing non-Newtonian behavior of blood with interpretation based on modified Stokes equation. Attributes of small sample volume, short measurement time and a single automatic process are thought be suitable merits as a blood viscometer in POC environment.

1. Introduction

A number of epidemiological studies attribute various pathogenic conditions to hemorheological properties including blood viscosity [1–15]. Erythrocyte aggregation, hematocrit, erythrocyte deformability and amount of plasma protein altogether affect blood viscosity [5,6]. Cardio-cerebrovascular disease [7–9], diabetes [10,11] obesity [12], hemorrhagic shock, oxidative stress [13] and renal disease are reported to have relation with increase in blood viscosity. For example viscosity increase in blood lowers blood flow which in turn deters insulin supply causing type 2 diabetes. Oxidative attack to erythrocyte membrane leads to increase in blood viscosity, which may manifest into vascular malfunction causing coronary artery disease [14,15].

Because of those significant implications of the blood viscosity in human health, many different types of viscometers have been utilized for medical purposes including rotational, capillary and falling ball viscometers [16–22]. However in spite of the importance of the blood viscosity as health information, widespread use of the blood viscosity has not been practiced due mainly to inconvenience and impracticability of the viscometers used today. Since those viscometers had been originally developed for engineering purposes, they mostly require large amount of sample volume, take multi-step processes and need to be cleaned at every measurement. For example although rotational viscometers have been most widely used in hemorheological studies, need for relatively large amount of blood sample and cleaning process at each measurement are thought to be the limiting factors for widespread use in clinical purposes [17]. Some new blood viscometers had been developed to overcome the disadvantages related with rotational viscometers. However they are still relatively complicated in their working structures and procedures [21,22].

Recently diagnostic devices aiming at point-of-care (POC) purposes have been drawing much attention due to manageability of the analysis process by an untrained personnel and applicability in an environment where regular medical services are not avail-

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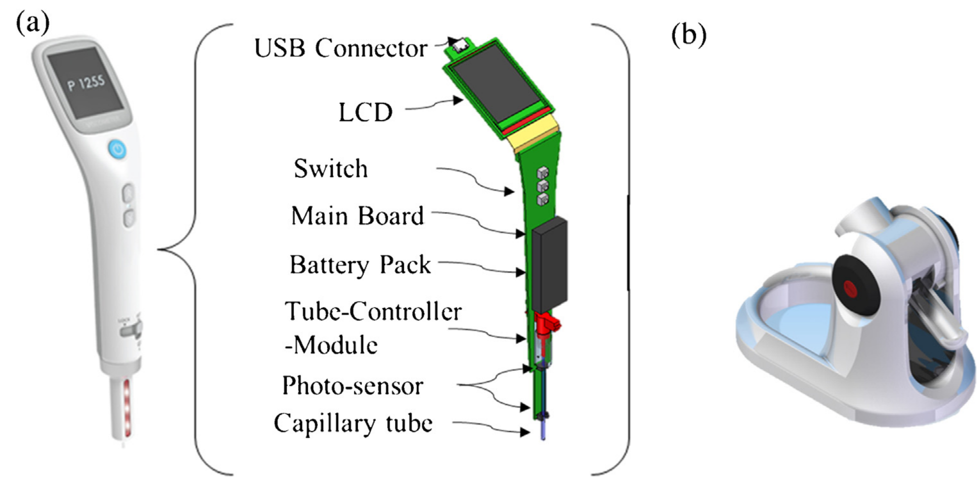

Fig. 1. Constituting parts of CFV: (a) the image of the main body of CFV with detailed descriptions of the components inside and (b) the cradle for the main body of CFV.

able [23–26]. Simplicity, rapidity, small sample volume, low cost and relative accuracy are the major attributes of the POC devices. Development of a blood viscometer that can measure viscosity within short period of time in a simple process with small sample volume is expected to contribute to enhancing usefulness of blood-viscosity measurement in POC environment. An interesting method for measuring blood viscosity was reported by measuring electrical impedance on an on-chip viscometer for POC application [26], based on the fact that the aggregation behavior of the red blood cell at lower shear rate increases the electrical impedance [27]. However the measurement requires separation of plasma before impedance measurement. Microfluidic rheometer was introduced to measure blood viscosity by determining shear rate as velocity of fluid and channel width were varied, considering blood as Newtonian fluid [28].

Considering the above-mentioned limitations of the blood viscometer, we propose in this report a novel hand-held viscometer device that can be potentially applied for measuring blood viscosity in POC environment. The measurement can be processed with a very small amount of sample volume (40 μL). The whole operation can be completed within a few minutes. Additionally the measuring process is very simple and easy with an automatic single-step process. Also since the capillary tube can be detachable, the used tube may be disposed after finishing the measurement process, obviating the need for washing and providing safer environment for the operator. These attributes of the CFV were able to be accomplished by installing a steel sphere inside a capillary tube, which can automatically start free-fall as the sample fluid reaches at the metal sphere at the upper part of the capillary tube. Fairly reproducible viscosity results were produced in qualitative and quantitative test for CFV. With advantage of easy handling together with dependability, CFV can potentially be applied as a medical device for measuring blood-viscosity in POC environment. In addition viscosity measurement by CFV was processed using blood samples, in which interpretation of the results based on modified Stokes equation produced non-Newtonian behavior of the blood samples.

2. Results and discussion

We developed a hand-held viscometer that can potentially measure viscosity of blood with a very small amount of sample volume (40 μL) within a few minutes. Fig. 1 shows the image of the CFV and its cradle. The detailed names of the constituting parts of the device are described which include a USB connector, a LCD, a start button, a main board, a battery pack, a tube connector, two photo detectors and a capillary tube. Measured values of the blood viscosity are displayed on the LCD panel. The start button enables controlling general functions of the device: to initiate and finish viscosity measurement, to retrieve the data previously measured and stored, and to supply and cut off power. The shape of the viscometer is designed considering convenient use for the operator. The cylindrical shape of the viscometer shaft provides convenient grip while the angled flat portion at the top part of the device serves to facile viewing position for the user. The viscometer may be charged using a commercial adaptor. Once the measurement is finished the capillary tube filled with the sample blood can be detached to be thrown away from the main body of the device simply by pushing the remove button. The facile detachability of the blood containing tube minimizes contact with the sample blood, providing safety of the handler. The device stand (Fig. 1(b)) is designed so that CFV may be placed firmly on its stand once the capillary is filled with the sample blood. The viscometer may be positioned on its stand with varying degrees of angles ranging from 10° to 90°. The versatility of the positioning angle provides diverse conditions of the measurement process allowing more precise analysis by increasing the detection time window when the viscosity measurement is processed at lower angle.

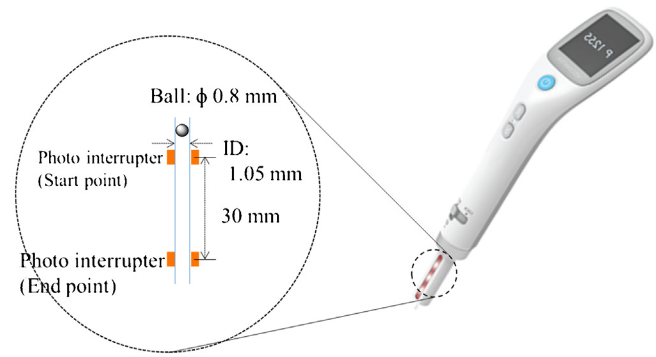

Fig. 2. A cartoon that describes the structural and functional description of the capillary tube with its placement in the main body of CFV.

The cartoon in the enlarged circle in Fig. 2 describes the detailed functional structure of the capillary tube. The total length of the capillary tube is 51.8 mm. The capillary tube is a transparent glass with inner diameter of 1.05 mm. A steel sphere is positioned at the top of the tube glued using BSA. The diameter and density of the steel ball is 0.8 mm and 7.8 g/cm^3 respectively. Photo interrupters are installed at both ends of the capillary tube with inter-distance of 30 mm. When the sample fluid is contact with the tip of the capil-