Development of a nonwoven filter for separation of serum from whole blood for medical diagnostic applications

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ABSTRACT

Analysis of whole blood in medical diagnostics often requires the removal of the red cells from blood samples. A new filter medium can remove red cells from blood leaving clear serum available for further analysis. The filter is a composite, wet-laid nonwoven containing cellulose, glass, synthetic staple, and synthetic binder fibers. Besides separating serum, the nonwoven filter exhibits high tensile strength for efficient automated converting and handling.

Application:

Composite filter media in a range of weights can provide diagnostic assays for blood proteins, lipids, and glucose with no significant bias of the analyte concentration being tested.

HEALTH ASSESSMENT OFTEN involves the analysis of blood samples using diagnostic screening devices, such as glucose or cholesterol monitors *(1)*. Such devices must frequently use serum—the uncolored fluid portion of blood containing analytes of interest to clinicians. Serum samples must be separated from whole blood before analysis to remove colored constituents of blood that could interfere with a colorimetric test or to reduce effects caused by variation in the red blood cell content (hematocrit) among samples.

It is possible to separate serum from whole blood in a centrifugation step, but the nature of rapid screening tests dictates that serum separation be an integral part of the test device. Prior strategies for rapid serum separation involved the use of one or more layers of glass fiber *(2, 3)* or membrane filters *(4)*.

Each approach had deficiencies, however. Membrane filters have little loading capacity and quickly occlude with application of undiluted blood. A wiping step is sometimes necessary to remove separated red cells from the membrane surface *(5)*. Although glass fiber filters have good loading capacity and separation efficiency, the delicate nature of binderless glass fiber filters makes device manufacture with automated handling difficult.

DESIGN GOALS

The characteristics needed in an efficient, rapid serum separation device include the following:

- Separation of red cells from serum by simple capillary or gravitational action
- No rupture of red blood cells (hemolysis)
- No binding or denaturing of serum components
- Single layer construction with sufficient strength for automated handling
- Transport of the serum to a collector or active site for further assay.

DISCUSSION

Wetlaid, spunbonded, and meltblown nonwovens were evaluated for the ability to separate serum from whole blood. The evaluation used three criteria:

- The ability to separate serum from whole bovine blood
- A rapid separation below 15 s as necessary in a diagnostic screening test
- A clean separation of serum from whole blood without hemolysis.

These evaluations showed that a defined porosity sufficient to retain red cells within the depth of the filter was necessary. An equivalent mean pore size of approximately 2.2 µm gave adequate separation of serum from whole blood. None of the standard materials we evaluated met all the criteria for adequate separation.

We decided to investigate composite wetlaid media using four different types of fibers to produce the needed characteristics *(6)*. The fibers selected for the medium were cotton linter fibers, glass microfibers, polyester (PET) staple fibers, and lower melting polyester binder fibers. Polyester staple fibers of 1.5 denier, 0.25-in. length were the backbone of the filter to provide the gross structure of the nonwoven. The cotton linter fibers provided a readily wettable capillary network to passively draw the blood through the filter. Glass microfibers of 0.40 µm mean fiber diameter produced the fine pore structure needed for red cell separation.

To increase strength, we added polyester binder fibers (PBF) to the furnish. Typical binders used in production of nonwovens interfere with the chemical reactions of some diagnostic systems. In addition, some

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binders may bind analytes of interest. Surfactants used to enhance wettability can also interfere with certain tests. Using a defined portion of PBF maintains the wettability of the filter. Tensile strength is sufficient for rewinding and the other necessary automated assembly steps of the diagnostic test kits.

The filter media used a furnish of 20% glass microfiber, 50% cotton, 20% PET staple fiber, and 10% PBF. Glass fibers were dispersed in a Hydropulper under acidic conditions. The cotton linters and synthetic fibers were dispersed in a beater. After mixing the fibers, the sheet was formed on a fourdrinier machine with light pressing. Controlled drying consolidated the web without total melting of the PBF.

Table I shows the characteristics of the filter. The table also shows comparisons to the separation characteristics of a binderless, wetlaid glass fiber filter.

Separation characteristics of serum from whole blood in the composite filter are similar to those of a binderless glass microfiber medium of similar thickness. Tensile strength is approximately 70% higher in the machine direction compared to a binderless glass fiber filter. This significantly enhances handling of the material. The total absorptive capacity is also significant. A similar glass fiber filter will absorb approximately ten times its own weight in whole blood. The composite absorbs about six times its own weight. The composite therefore requires a smaller volume of blood to fill it. This is important for applications involving fingerstick blood samples—often used in rapid diagnostic formats—where the amount of blood available for assay is small—often less than 20 µL.

	Composite medium	Glass fiber
Weight, g/m^2	77	56
Thickness, mm	0.33	0.30
Capillary rise, mm/60 s	49	52
Tensile, dry, kN/m		
MD	0.63	0.37
CD	0.37	0.28
Absorption time for bovine blood, s/50 µL	7.7	7.0
Separation for bovine blood, mm/50 µL	2.8	3.0
Capacity for bovine blood, % by wt.	630	1040

I Comparison of composite medium to binderless glass microfiber

CONCLUSIONS

Composite filter media have been made in four different weights in the range 40–225 g/m^2 with corresponding thicknesses of 0.18–0.95 mm. Materials were evaluated in diagnostic assays for blood proteins, lipids, and glucose. They did not significantly bias the analyte concentration being tested. Tests included both human and bovine blood. Machine handling, rewinding, and automated kit assembly were satisfactory.

Further work continues to identify ways to improve the serum separation efficiency of composite media. Human hematocrit values at the upper range of the normal distribution have presented a problem to serum separation efficiency due to the higher volume of red cells per unit of whole blood. Other fibers, fiber distributions, or chemical treatments may provide improved rapid serum separation materials for whole blood diagnostic tests, however. TJ

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