News Feature

INSTANTANEOUS BLOOD TYPING USING PAPER DIAGNOSTICS

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Blood is essential for sustaining living tissue by supplying oxygen and other soluble nutrients to provide stable colloid suspension made of red blood cells, white cells and platelets dispersed in an aqueous solution (plasma) containing a host of biomolecules (fatty acids, hormones, etc). Detection blood type is critical for transfusion as well as many medical procedures. Blood analysis is also important in veterinary medicine. Different blood typing techniques are available: gel column, thin-layer chromatography (TLC)-immunostaining, spin tube method, fiber optic-microfluidic device, etc. Among those, the identification and automation of red blood cell agglutination by antigen-antibody interaction often requires optical or microfluidic analytical instruments. However, there are no robust and convenient low cost disposable tests available for "on the spot" analysis of blood type. Blood samples are typically outsourced to an analytical laboratory. Reliable instantaneous test critical blood analysis without requiring sophisticated laboratory analytical instrumentation would be invaluable for improving health in the underprivileged/remote areas of the world.

A Bangladeshi scientist, Dr. Mohidus Samad Khan and his co-researchers recently developed paper based diagnostic devices for instantaneous blood typing from Monash University, Australia. They found that agglutinated blood transports differently onto paper than stable blood with well dispersed red cells. They investigated this difference to develop blood typing tests using specific antibody-antigen interactions to trigger blood agglutination.

As a blood donor, Dr. Khan comprehends the importance of instantaneous blood typing; a single-step blood typing technique can be very much useful in different occasional blood collection camps as well as emergency medical situation.

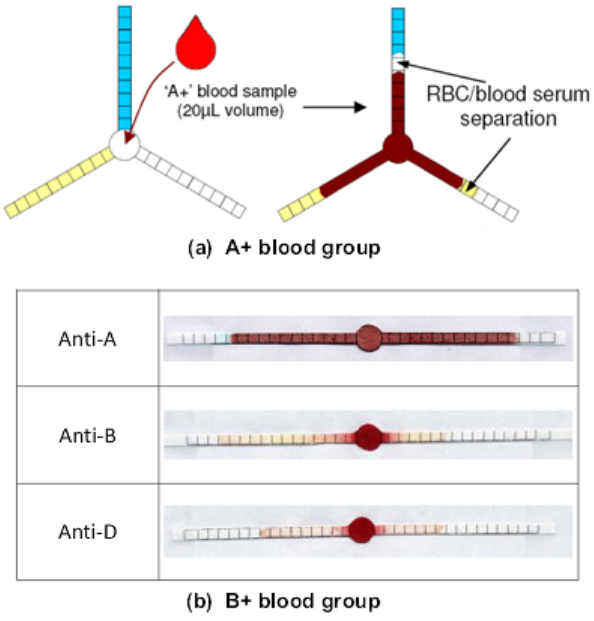

Figure 1: Blood group detection techniques using paper diagnostics (Khan et al, 2010)

A Biosurface/Biochemical Engineer by profession, Dr. Khan completed his BSc in Chem Eng form BUET, Bangladesh and PhD from Monash University, Australia. His PhD thesis was on Biosurface Engineering entitled: 'Bioactive Papers: Printing, Activity and Stability'. Currently he is working as a research fellow in McGill University, Canada. His research focuses developing cheap manufacturing of high quality bioassays for health and environmental applications and low cost paper diagnostics.

In his PhD project he investigated the activity and stability of biomolecules deposited on paper. His research showed that biomolecules such as enzymes can be two to three orders of magnitude more stable than that in solution. He used paper as substrate since paper is biodegradable, biocompatible, easy to functionalize, easy to sterilize, cheap and available. This finding instigates the idea to develop single-step paper based blood detection device. After primary investigation of the concept, Dr. Khan consulted his PhD supervisor Prof. Gil Garnier. Prof. Garnier is a renowned researcher on colloid and interface science and a visionary leader. He appreciated the potential of the technique and gave full support to conduct the research.

Working with blood samples requires specialized labs and collecting blood samples from volunteers or pathological labs is time consuming. Dr. Khan started with his blood sample to kick off the experiment (followed by Dr. Thouas and Prof. Garnier in later stages) and tested on different antibody (A, B, D) treated papers. Dr. Farzana Mazid, a local GP (general practitioner), helped collecting blood samples. The preliminary results successfully qualified the concept that blood wicks differently on specific/non-specific antibody treated papers.

With the primary results, Prof. Garnier and Dr. Khan established research collaboration to Dr. George Thouas of Monash Immunology and Stem Cell Laboratories (MISCL), Dr. Wei Shen from Chemical Engineering and Prof. Gordon Whyte of Faculty of

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Medicine, Nursing and Health Science, Monash University, Clayton. Dr. Lisa Collison from Monash University Health Service helped to collect blood samples from volunteers (researchers and colleagues).

The next critical step was to use the blood wicking behaviour on specific/non-specific antibody treated papers and amplify the signal so a user with limited knowledge on haematology can even understand the result. The research team optimized the design of paper fluidic channels for blood typing. They came-up with two different techniques to detect blood type using paper diagnostics: the first technique analyzed the wicking and the chromatographic separation with specific and nonspecific antibodies. And the second technique relates the level of agglutination and the fluidic properties of blood on its transport in paper.

In the first technique, blood droplet was deposited onto paper strips pre-treated with specific and nonspecific antibodies. Blood agglutinated by interaction with its specific antibody(ies) cause a chromatographic separation. The red blood cells wicked very little while the plasma wicked at a faster rate than the original blood sample. From the chromatographic separation in presence of specific antibody(ies) blood type can be detected accurately. The researchers showed a three arm prototype for single-step blood typing.

In the second technique, blood samples were mixed at specific ratio with specific and nonspecific antibodies and a droplet of each mixture was deposited onto a filter paper strip. Agglutinated blood phase separated, with the red blood cells forming a distinct spot upon contact with paper while plasma wicked; in contrast, stable blood suspensions wicked uniformly.

Both the techniques can be used from home or pathological labs; and most importantly the test can be done for a few cents.

The research team acknowledges Dr. Farzana Mazid, Roland Lee and Nazlee Sharmeen for technical discussion; Sharon Haniffa and Karla Contreras for assistance in the lab; Lisa Collison from Monash University Health Service and all the volunteers who contributed in this project by donating blood samples.

According to Dr. Khan, it is important to transfer the technique from the research lab to the community so that a regular person from a remote area can purchase a paper diagnostics from a pharmacy/chemist-shop and perform blood testing of family members or stock following instruction written behind the packet. The product should be manufactured and distributed in industrial scale. He and the co-researchers filed Patent Application aiming industrial production of paper diagnostics for blood typing. This work has recently been published in Analytical Chemistry, a prestigious scientific journal. Dr. Khan believes their work will open a new horizon to the researchers and will lead the development of different pathological tests, yet restricted in well equipped pathological labs, using much convenient paper diagnostics. However, it is important to do more research especially on the aging of paper diagnostics at different operating conditions.

Related publication/patent can be found at:

- **M.S. Khan**, G. Thouas, G. Whyte, W. Shen, and G. Garnier (2010) “Paper Diagnostics for Blood Typing”, Analytical Chemistry 82(10), 4158-4164. doi: 10.1021/ac100341n
- **M.S. Khan**, X. Li, G. Thuas, W. Shen and G. Garnier, “Paper Based Diagnostics for Blood Analysis and Typing”, applied for Australian Provisional Patent 2009904643, 24 September, 2009.