

Research Article

Improvement Study on Blood Test Investigation by Nanoparticle-Coated Colour-Coded Sample Paper

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Nanobiotechnology is a growing branch of research that combines biology and nanotechnology to study and create unique, functionalized nanobiosystems. This interdisciplinary study subject has significant promise for improving medical engineering. Finding the exact blood category is a coercive test for blood transfer and other incalculable health checkups. The pandemic has accelerated these test frequencies in an exponential fashion. It is usually the job of the practitioners working in the laboratory to name the types of blood samples. Depending on the blood type and its cross-matching fitness, recommendations are offered for blood transfer. In many places, this type of testing is done manually, and it is done through a microplate and test tube. These tests usually take longer, and the chances of errors are high, which can lead to fatalities. Polymer-based paper sample collection has been shown to be ideal instruments for conducting blood tests in response to this requirement because of their capacity to do quick and low-cost diagnostics and analyses. In this paper, a novel nanocoated blood polymer sample paper with unique coding was proposed and investigated for its operational simplicity and effectiveness. A unique coded polymer sample paper has prevented complications during blood tests and provides expected results without errors.

1. Introduction

Nanotechnology, one of the most fascinating fields of science, provides scientists with the power to make, manipulate, and utilize materials on a nanoscale, making it one of the most exciting research areas. Biotechnology has aided in transmitting information about biological systems to the industrial sector. The various physicochemical and biological features of nanoparticles have also led to the use of nanotechnology in a variety of healthcare settings [1]. Nanobiotechnology is one of the most recent developing branches of research, and it is the interface between biology and nanotechnology, studying and designing unique functionalized nanobiosystems. This interdisciplinary study topic offers tremendous promise for advancing medical engineering technology [2]. In 1616, the English physician William Harvey discovered the existence of blood circulation in animals. He also discovered that blood could be transferred from one animal to another because it circulates here and there in an organism. In 1665, English physician Richard Lowe examined blood transfusions in dogs. In the nineteenth century, physician James proposed that humans donate blood to compensate the blood loss during surgery. During his study, physician Leonard Landois discovered that when red blood cells were transfused from one species of animal to another, they usually clumped and sometimes scattered. Further, he reported that injecting a person with a different type of red blood cell would cause his or her urine to turn black. Through this, he scientifically proved that transferring blood from one species to another could be harmful. In 1901, an American biologist, Karl Landsteiner, discovered the presence of ABO blood groups in humans by birth in Austria. He also discovered the existence of antigens and antibodies in the blood. Further, when one type of blood mixes with another type of blood, these substances trigger the red blood cells to appear to merge [3].

A year later, some other researchers diagnosed a fourth type of AB blood type. Red blood cells combine when transfusing type B blood to a person with type A or transferring type A blood to a person with type B. The same result can be seen when injecting AB type blood into a person with type A or type B blood. Usually, when type O blood is mixed with other blood types, it does not coalesce and remains normal. This knowledge of blood types is essential because if mistakes are made, they can lead to loss of life. Blood cross-matching can be done to find out if a person's blood is suitable for another. Most people in Great Britain and Northern Ireland routinely donate blood voluntarily [4]. Moreover, an average of two million units of blood per year are used for transfusion. The blood should be used in an appropriate manner as it can be donated in small quantities by one person at a time. The use of blood transfusions can be best managed using the Maximum Surgical Blood Order Schedule (MSBOS) during surgery [5]. The number of required blood units for each operation is calculated according to the traditional analysis method. Before surgery, the quantity of blood units a patient needs can be booked on a cash basis in real time. It allows us to accurately calculate the number of blood units needed in an emergency [6]. The British Committee for Standards in Hematology has given the world the practical guidelines needed to perform blood transfusions properly [7]. It is necessary to verify that the blood transfusion is correctly done through a compatibility test based on a patient's past blood transfusion history, cross-match, ABO, Rh combination, and suitability of antibodies for both the blood giver and the patient. The blood level similarities and conflicts between the blood giver and patient can be identified through the cross-match test. Usually, this type of information is not available through blood group typing [8]. It was reported that, traditionally, the anti-IgG tests performed had been done in an unsafe manner compared to the computerized cross-match test. Further, all computer-assisted blood test results are stored on the computer, which reduces the possibility of human errors, and thus, the cost of the process is also reduced. At the University of Michigan Medical Center, the most notable event is the blood transfusion without any errors being found from the results of one lakh, 38 thousand crossmatch tests conducted with the help of a computer [9].

The blood has the potential to be a window into one's health, and as a consequence, it is the human biofluid that has been researched the most. Blood tests may be used to diagnose disorders, evaluate the effectiveness of treatment medications, and gather information about a person's overall health. It is becoming more critical to do rapid reaction blood tests when following therapy is necessary. Paperbased devices have been shown to be ideal instruments for conducting blood tests in response to this requirement because of their capacity to do quick and low-cost diagnos-

tics and analyses in a nonlaboratory setting. In this perspective, we discuss recent advancements in paper-based blood testing, with a particular emphasis on the individual methodologies and assays that have been used in each case. Additional topics covered in this study include how to increase the signal intensity of these paper-based devices and leverage in situ synthesis of nanomaterial to improve the sensitivity, functionality, and operational simplicity of these devices in the future. As a result of these developments, paper-based devices are becoming more viable instruments for performing point-of-care blood tests in a variety of real-world situations. The purpose of this article is to look at the issues that may arise during blood grouping tests and cross-matching tests and how to deal with such problems effectively. The proposed method eliminates the complications that occur during manual blood grouping. In this research, the nanoparticle of titanium oxide- (TiO₂-) coated blood sample polymer paper with unique coding was proposed and investigated for its operational simplicity and effectiveness on blood test investigations.

2. Blood Group Investigation

Before transfusing blood from one person to another, one needs to find out the blood types of the donor and receiver and then find out the cross-match between the two. Individuals who perform these experiments are certified in this domain and have experience in training. The practitioner will decide whether or not to use one's blood based on the results of the cross-match test. If the results of the crossmatch test are appropriate, the blood transfusion between two people will be allowed; otherwise, it can cause the patient's immune system to fail to function appropriately and sometimes even result in loss [10]. This type of test is usually needed when the hemoglobin level in the blood is low, when there is a disease in the blood cells, or in cases where the blood is not stopping or going for tissue transplantation. In medical emergencies, doctors usually choose O type blood, also known as universal blood type, for blood transfusion. If it is entirely free of antibodies at the end of the cross-match test, then it will be selected as the best suitable blood. In a few cases, a low number of antibodies will be found at the end of the test, and it will be tested further to determine its suitability. It is completely eliminated when antibodies are found that usually cause side effects. Direct handling of blood samples should be minimized when performing these types of tests because sometimes there is a chance that some samples may have some pathogens, so the chances of the pathogen being infected are very, very high [11].

There are some flaws in the cross-match. There is no guarantee that the red blood cells that were first transplanted will enter the patient's body and live well. This test, performed on a patient's serum, does not detect unexpected red blood cell antibodies. An unknown drug injected into a patient's body will break down the patient's red blood cells and antibodies in the patient's body, which cannot be prevented by a cross-match test [12]. Furthermore, the test does not reveal any details about other diseases in the donor's body or the recipient of the blood. Most importantly, these blood samples must be collected and tested within three days; otherwise, we will not be able to obtain accurate patient information. The room temperature of the laboratory where this test is being performed should not exceed 37 degrees Celsius so that we can easily see the clumping antibodies [13].

The donor's or recipient's serum is used to determine if there are any antibodies attached to the cells that are not appearing as a group. The cross-match test with the addition of polymerized albumin improves the performance. The computer-assisted cross-match test is performed on the serum and the donor's blood. This test requires only a small amount of blood [14]. During this test, the patient's blood must be in the laboratory [15–17].

Between December 2013 and December 2016, a study was conducted at the Indus Hospital Blood Centre, Pakistan, which showed 45,425 donors. Of these, a total of 413 blunders were detected. Here, human errors were spotted by computer-based blood bank management software that could run with the help of the website. Looking at the literature reports mentioned above confirms that the errors that occur in the laboratory persist. The primary purpose of this research is to look at how manual tests can be ruled out, such as naming blood groups, transfusions, and cross-match testing errors. It will save a great deal of time and human lives. Observational research was done at the Yazd Blood Transfusion Center between March 2010 and March 2017 and reported by Napier et al. [18]. The blood types of all the donors were tested by test tube and were considered the number of blood transfusions during the eight years mentioned above which was three lakh twenty two thousand, of which about 130 cases were misdiagnosed. The percentage of these errors is approximately 0.04% [18].

3. Existing Methodology

Many types of strategies and observations are employed for naming blood in general in medical laboratories. However, many of them are concerned with the appearance of test results. Here, we look at the pros and cons of the slide method.

3.1. Slide Method. The slide test has much lower sensitivity compared to other tests that detect blood types. However, this test is very effective in emergencies as it gives accurate results. A glass plate is divided into three regions during the test; one drop from the donor's blood and one drop from the recipient's blood are mixed with antigens A, B, and C separately. This test lasts five to ten minutes and can detect the formation or scattering of blood platelets by which blood type is determined. However, it is very difficult to diagnose blood types with blood samples that are less reactive to antigens. Slide tests are beneficial for detecting blood types outdoors, but blood transfusions based solely on the results obtained from slide tests may not be safe [6]. Beyond all of this, all the test results will be taken incorrectly if the technicians sometimes mistakenly put this glass plate upside down while performing this test. There are some new ideas in this article to help with the problems that come up because of the changes.

3.2. Glass Slides with Colour Code Marking. During a blood type test, three drops of red blood cells are taken at different points on a piece of glass. The three antigens, A, B, and anti-D, will be added separately with the samples taken and observed in Figure 1. The antigen combined with blood cells reacts and turns into agglutination; otherwise, it remains the same. Blood types are classified according to this. Hundreds of samples of such blood types in laboratories are handled simultaneously, and laboratory assistants are more likely to place the plates in an upside down position when handling them. It will become erroneous when deciding the tests of the samples thus placed.

3.3. Error Data. Errors that occur when using this existing method are studied. For this purpose, three blood test laboratories in small towns near Madurai, India, were considered. The following is the study report taken from January 2019 to December 2019.

Table 1 shows the results of the blood test. The tests are conducted at three blood test centers. Table 1 covers all the results of tests conducted in those centers during 2019 that have been taken into account. Of these, 1348 tests were performed at Vickram labs (test lab I), 923 tests at the Siva X-ray Center (test lab II), and 2345 tests at Vaigai Raj Scan (test lab III). When you look at the results of this table, it is clear that something went wrong. The results of seven tests in the test conducted on the Vickram labs were incorrectly identified. Similarly, three tests were incorrectly reported at the end of one-year tests conducted at the Siva X-ray Center. In addition, out of 2345 tests conducted on the Vaigai Raj Scan, the results of about seven tests were incorrect. In particular, a test conducted at the Vickram lab misdiagnosed two people with A-ve blood types as O+ve and five people with B+ve blood types as AB-ve. In the same way, a test at the Siva X-ray Center misidentified three people with O+ve blood types as A-ve and one person with an AB-ve blood type as B+ve. Similar confusion occurred in the Vaigai Raj Scan as well, where four people with A-ve blood types were diagnosed as O+ve and three people with B+ve blood types were reported as AB-ve.

When examining how errors occurred in the results of these experiments, it became apparent that technical errors were the cause. These errors occurred while the test was being performed with the test microplate upside down. For example, if the plate with an AB-ve blood type shown in Figure 1 is turned upside down, it will be B+ve. A new attempt to fix this problem has been made, and its results have been successful. Figure 2 compares the error rates of the three selected blood test canters in 2019.

4. Nanocoated Paper with Colour Code Marking Method

There are several applications for titanium dioxide nanostructures, including medical, energy, and biosensing, to name a few. For biosensor applications, the use of TiO_2



FIGURE 1: Blood test samples for AB negative blood and B positive blood using glass plate.

TABLE 1: Comparison of blood test results (actual vs. reported) during 2019.

Name of the lab	No. of blood tests in 2019	Blood test types (actual)									Blood test types (reported)							
		O-	O+	A-	A+	B-	B+	AB-	AB+	O-	O+	A-	A+	B-	B+	AB-	AB+	
Test lab I	1348	13	535	5	342	3	356	2	92	13	537	3	342	3	351	7	92	
Test lab II	923	2	395	1	241	0	202	1	81	2	392	4	241	0	203	0	81	
Test lab III	2345	23	905	9	667	9	524	7	201	23	909	5	667	9	521	10	201	



FIGURE 2: Comparison of error rate.

nanostructures has resulted in significant improvements in target detection. Titanium implants have poor contact with the surrounding tissues, and TiO_2 nanostructures are a good way to make up for this problem by making nanoporous surfaces and complex structures. Nanotechnology has produced a variety of valuable nanostructures for biotechnological purposes, the most common of which is nanosized titanium dioxide. Nanostructured TiO_2 can be used in a lot of different ways because of its low toxicity, good biocompatibility, and own properties [19].

Nanostructured TiO_2 seems to be inert and harmless when exposed to the human body. Biomedical device development will be aided by a thorough knowledge of nanoscale phenomena, which may be used to create antimicrobial surfaces, implants, and more. To better understand how TiO_2 nanoparticles are being used for biomedical purposes today, this study will concentrate on the most recent developments in that field's utilization and the most critical aspects that impact TiO_2 's biocompatibility and the difficulties that lie ahead. Traditional disinfection techniques are not as successful as photocatalytic procedures. Therefore, TiO_2 coated surfaces with antibacterial qualities might be used in the healthcare business. Because TiO_2 -coated catheters are safe and have the potential for light disinfection for clinical usage, they are another interesting use of TiO_2 in biomedicine [20].

During a blood type test, three drops of red blood cells are taken at different points on a piece of glass. The three antigens (A, B, and anti-D) will be added separately with the samples taken and observed. The antigen combined with blood cells reacts and turns into agglutination; otherwise, it remains the same. Blood types are classified according to this. Hundreds of samples of such blood types in laboratories are handled at one time, and laboratory



FIGURE 3: Nanocoated polymer-based sample paper with colour code marking.



FIGURE 4: Blood samples on nanocoated polymer paper with bar code.

assistants are more likely to place the plates in an upside down position when handling them. It will become erroneous when deciding the tests of the samples thus placed [21].

A new colour-coding system has been introduced to eliminate such mistakes. That is, colour coding similar to the colours of the antigens is attached to the side of the nanocoated paper, as shown in Figure 3. This allows laboratory assistants to insert the exemplary antigens in the right place during the test to correctly record the results. A bar code is attached to the top of the blood sample polymer paper as shown in Figure 4.

Tests were performed at all three centers again for a period of six months by attaching colour coding to a microplate that can be used for blood type. The results of this test are shown in Table 2.

Many researchers [22–26] tried the sampling through paper-based biological tests and succeeded in their investiga-

tions. The blood paper slide is made of nanocoated paper with a thickness of 0.28 mm and is pasted on the card board pierced with a circular brim to prevent the blood dot from escaping sideways. The four coloured dots, as per the standard provided on the board, are to mix the blood with various antigens and to see the result. The gelatin-coated layer on the slide prevents blotting of the blood liquid. After usage, if the slide is incinerated, there are no harmful chemicals emanating through combustion, thus preventing pollution in the atmosphere. Each slide card is provided with a barcode to identify the particulars of the patient. The results show that errors are reduced with the help of the proposed colour-coding method. Blood type tests performed during the study period using the proposed colour-coding scheme proved that there were no technical errors. There is a small cost to driving the colour pieces on the microplate that can be used in a blood classification test using this method, but significant damage is avoided.

TABLE 2: Comparison of blood test results (actual vs. reported) during 2021.

Name of the lab	No. of blood tests in 2021	Blood test types (actual)									Blood test types (reported)							
		O-	O+	A-	A+	B-	B+	AB-	AB+	O-	O+	A-	A+	B-	B+	AB-	AB+	
Test lab I	533	9	207	5	138	4	127	1	42	9	207	5	138	4	127	1	42	
Test lab II	412	3	169	2	111	1	103	1	22	3	169	2	111	1	103	1	22	
Test lab III	1107	2	416	1	321	2	287	1	77	2	416	1	321	2	287	1	77	



FIGURE 5: Blood group identification on nanocoated paper.

When supporting materials have adhered to a polymer paper sheet, nano-TiO₂ may be utilized as a retention agent to keep them in place. Concerning the retention agent, there are two possible mechanisms: coating with a nano-TiO₂ suspension on the sheet surface and wet end addition, in which nano-TiO₂ is deposited onto individual fibers prior to sheet formation, resulting in an even distribution of TiO₂ loading throughout the sheet [27]. For example, when nano-TiO₂ was combined with hexadecanoic acid, the surface characteristics of the combination revealed a significant improvement in wetting and dispersion. The polymer paper containing nano-TiO₂ showed a greater dynamic elastic modulus than the empty papers. There is a new way to make high-tech polymer paper with a superhydrophobic surface made by adding modified nano-TiO₂ to cellulosic fibers [28].

The absence of an evident agglomeration phenomenon between the coated particles suggests that the TiO_2 particles may be effectively coated on the blood sample polymer paper when the blood sample papering process was used. In this case, irregular morphologies of the coated TiO_2 particles might explain the uneven surface structure of the produced paper. The results of the blood being deposited on the surfaces of both uncoated blood sample paper and

TiO₂-coated polymer paper (Figure 5) for the creation of spots are remarkable in that a substantial difference was noticed between the top and rear surfaces of both paper substrates [29]. The blood sample paper demonstrated that the applied bovine blood penetrated consistently through the paper substrate. The diameters of the spots on the top and rear sides showed a similar value. The minimal variation between them reveals that the colour of the backside of the paper substrate inside the spot region was somewhat darker than the colour of the top surface. As shown in Figure 6, when blood was deposited on TiO₂-coated polymer paper, the blood sample was utterly blocked on the top side of the paper substrate, and there was no prominent blood sample visible on the backside of the paper substrate, which is in contrast to the performance of the commercially available polystyrene base paper [30].

To our understanding, the surface characteristics of the one-sided TiO_2 -coated polymer paper might be responsible for this event. After the blood sample was placed on the coated paper, it would interact directly with the TiO_2 particles coated on the top side of the blood sample paper's cellulose fibers, therefore enhancing the experiment's effectiveness. This may be advantageous for the analysis of target



FIGURE 6: Blood identification on nanocoated paper [21].

chemicals in spots because of the high capacity of the coated TiO_2 particles, which adsorb blood onto the surfaces of these particles and make it difficult for the blood to pass through the paper substrate on the other side [31]. At the same time, higher concentrations of blood samples between the edge and the center of the spot were observed from the photographic image of the spot on the TiO_2 -coated polymer paper, which could be an issue when a subpunching strategy is used. A nonwhole spot is analyzed due to the nonuniform distribution of blood samples on the TiO_2 -coated polymer paper.

4.1. Environmental Impact of Bioclinical Waste. Bioclinical waste is a significant source of hazardous biomedical waste creation globally. The development and disposal of medical waste is an essential consideration, particularly in nations with poor hygiene and a large population. Medical facilities, such as hospitals, clinics, and other locations where diagnosis and treatment are provided, create hazardous trash and put individuals at risk of contracting life-threatening infections. Policies should be developed to prevent the spread of infectious diseases by specifying how waste should be handled throughout the stages of creation, segregation, collection, storage, transportation, and treatment. It is necessary to raise awareness at all levels of society, using various communication and educational tools, to reduce the likelihood of the health dangers spreading. Healthcare waste includes potentially hazardous bacteria that can potentially infect hospital patients, healthcare employees, and members of the public at large [32–34].

The most common issues associated with healthcare waste are a lack of awareness of the health risks associated with waste generated during medical procedures, insufficient training in proper waste management, a lack of waste management and disposal systems, a lack of financial and human resources, and a lack of priority given to the issue of waste generated during medical procedures. Many nations either do not have enough rules or do not enforce those that exist [35–38].

Safe and sustainable management of biological waste is the social and legal duty of everyone who participates in, supports, or provides financial support for healthcare operations. Effective biomedical waste management is essential for the health of individuals and the preservation of the environment. The blood sample paper is biodegradable. Biodegradation of biomedical waste is a more efficient and cost-effective procedure than any other traditional method of biowaste disposal. It is also more environmentally friendly [39, 40].

5. Conclusion

It is the social and legal responsibility of everyone involved in, supporting, or giving financial support for healthcare activities to ensure the safe and sustainable treatment of biomedical waste. This blood type test is essential today as the population increases and diseases are also on the rise. Especially in this pandemic period, many people around the world have been subjected to this blood type test. It is challenging to do many tests manually, so mistakes are severe. Laboratory assistants were employed over time in hospitals, in many laboratories, and in many places. From the study, it is proved that this novel attempt prevents complications during the blood test. Moreover, this system provides an accurate result, saves time, and slightly increases the cost. The next step in this endeavour is to test this nanocoated polymer paper with the help of a computer system. Also, by fitting the barcode on this polymer paper, the details about the patient can be known accurately. Nanocoated blood sample polymer papers avoid clerical errors that may occur during blood tests and save valuable human lives. This polymer-based paper also helps to preserve the environment by replacing glass slides as biomedical waste.

Data Availability

The data used to support the findings of this study are included in the article. Should further data or information

be required, these are available from the corresponding author upon request.

Disclosure

This study was performed as a part of the Employment Hawassa University, Ethiopia.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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