JFatwa
ISSN: 2232-1047
eISSN: 0127-8886
Journal of Fatwa Management and Research
مجلة إدارة وبحوث الفتاوى | Jurnal Pengurusan dan Penyelidikan Fatwa

SeFPIA 2018 | SPECIAL EDITION
ISSN: 2232-1047 eISSN: 0127-8886

REVIEW ON MICROFLUIDIC PAPER BASED ANALYTICAL DEVICES (μPADs) AND POSSIBLE APPLICATION BY EMPLOYING WASTE PAPER

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Abstract

Microfluidic paper-based analytical devices (μPADs) has been broadly used and gained many researchers attention for clinical medicine and health, food quality inspection and environmental analysis. Qualitative analysis on several related articles managed to review the development of μPADs and as a result the proposal on its fabrication techniques by using waste paper for the application in environmental analysis through colorimetric detection is determined. The deinking process of waste paper can be carried out by using enzymatic treatment while the fabrication of μPADs can be carried out by using wax printing technique. Therefore, the device is subjected to be tested with detection of metal ions from water sample through colorimetric detection.

Keywords: *μPADs, enzymatic treatment, waste paper, metal ions and colorimetric.*

INTRODUCTION

Recently, the attention towards the development of microfluidic paper-based analytical devices (μPADs) has grown rapidly for global health care which act as a diagnostic devices. μPADs were brought in into this world in the year of 2007[1]. According to Lei et al. (2012) many activities in conventional analysis system such as sample manipulation and identification can be operated on a piece of paper[2]. This device have characteristic of hydrophilic or hydrophobic micro channel-networks and connected analytical devices that can permit fluid conducting and quantitative analysis for its applications in some field for instance medicine, healthcare and environmental analysis.

μPADs were very popular these days due to their low expenditure, simplicity, adaptability and disposability as stated by (De Oliveira et al., 2017)[4]. This analytical device can afford a helpful and without delay response to a patient's test sample. μPADs can be fabricated using a simple, transportable, compact and handheld instrument. μPADS is convenience for blood testing or urine testing for detection of desired compounds. For instance, glucose, cholesterol, pathogens, blood gas, coagulations, haemoglobin, pregnancy and others.

μPADs have attracted many researcher attentions for its ability in sensing multiple analytes, verifying analytical test results, quick sample analysis and reduce the capacity of samples and analytical reagents. Lim et al. (2017) expressed that μPADs which can offer accurate and dependable precise measurement without sample pre-treatment can ease patient medical problem and generate quick test results thus assisting doctors in deciding proper treatment[5].

PAPER BASED DEVICES

Paper is now acknowledged as an attractive and capable substrate material for microfluidic application due to its tremendously low cost, ubiquity, flexibility, lightness and low thickness.

Paper recycling has been practiced for many decades in abundant nations around the globe. The recycling processes turn out to be gradually efficient with rapid improvements being made in deinking processes for the reuse of the secondary fibres. Nowadays, almost all types of paper are manufactured from recovered paper [6]. Most recovered papers are used to generate brown grade papers and panels. However, in the past two decades there has been an extensive growth in the use of recycled paper to produce white grades paper through deinking such as newsprint, tissue and market pulp.

In addition, recycling paper will reduces methane and carbon dioxide in the atmosphere. Recycling is very essential as waste has a massive adverse impact on the natural environment.

Paper has been used for many applications over the millennia, and recycling of paper has been feasible for over a century. Paper has become more and more prevalent around the globe.

Over the time, with the growth of nanomaterial and nanofabrication technologies, numerous attracting and inventive ideas and models for μPADs have been recorded. According to Shah et al. (2013) paper is considered a very interesting platform for non-refundable diagnostic devices because of its exclusive properties which include easily accessible and produced in every part of the globe at very low-priced. Beside, paper is biodegradable, stretchy, simply coated and printed[7]. Paper is composed of a spongy cellulose arrangement, so it acts as a filter for various analytical purposes and it is normally white.

Hydrophobic component in hydrophilic paper are the basic concept of μPADs invention where Martinez et al. (2008) discovered the field by patterning chromatography paper through photolithography. Subsequently, a progression of innovative techniques of patterning paper such as wax printing, inkjet printing, laser printing, flexographic printing, paper stamp based printing, plasma etching, laser treatment, cutting and mechanical plotting have been developed[8]. Then, a technique using permanent marker with particular pattern or also known as porous pen which employ water resistant ink and consists of colorant, a solvent (ethanol) and a hydrophobic resin has been invented. It can form long-lasting marks on a variety of surfaces such as plastic, stone and metal by directly plot μPADs with the support of iron templates through designed patterns that are produced by a traditional laser cutting technique. The ink can pass over the paper body where the residual of resins from a very quick evaporation of the solvent will produce hydrophobic walls to guide the movement of fluid through the paths. The process is schematically shown in Figure 2.1.

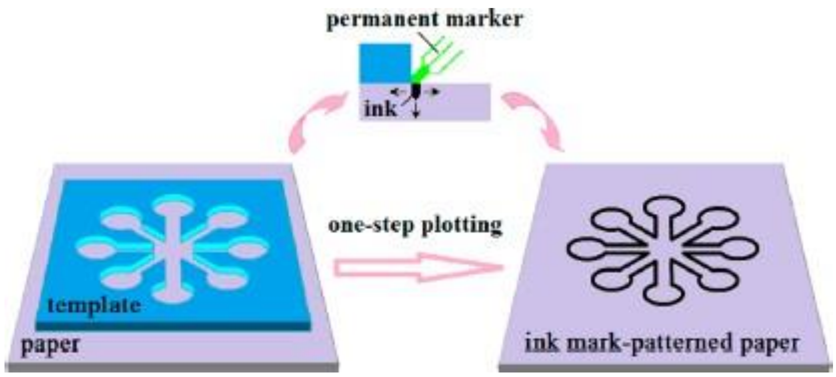

Figure 2.1: Schematic of the one step plotting method for patterning papers[8]

Basically, fabrication of μPADs can be parted into two methods which are 2D and 3D method to transport fluids in both horizontal and vertical dimensions which rely upon on complexity of the diagnostic utilization[1].

According to Tsatsis et al. (2017) recently, vast quantities of paper are being used in households as well as in working places, industries, school and in all domains of life[9]. Next, there are many methods for the development of μPADs but it is unknown if wax printing methods is suitable and convenient for waste paper. Hence, there is no research that showed the development of μPADs from waste paper.

APPLICATION OF MICRODLUIDIC PAPER BASED ANALYTICAL DEVICES (μPADs)

As mentioned early, the application of μPADs as a diagnostic devices is crucial and important because of its characteristics which is easy to use, portable and economical. Beside, μPADs is an economical diagnostic devices that can be produce in a large quantity but reasonable for the user. Consequently, in resource limited area, μPADs can be used for inspecting and controlling illness and environmental pollutions.

In industrial applications, sensor is one of important technology as it being used for process control, analysis and safety and also for medicine, it is being used for diagnostics, critical care and controlling. The application of μPADs is summarized in Table 1.

Table 1: Application of μPADs.

Field	Application	References
Medical and forensic analysis	For plasma separation and SERS measurements	[10, 11, 12]
	Analysis of glucose, nitrite, uric acid and protein	[3, 5, 10, 13, 14, 15, 16]
	Detection of H_2O_2 and glucose	[1, 2, 10]
	Detection of human chorionic gonadotropin and humoral antibodies	[1, 17, 18]
	Urinalysis	[4, 13, 18, 19, 20]
	Pathogen and drug analysis	[7, 19, 21]
	Cancer detection	[7, 12, 22, 23]
	Pregnancy test	[24, 25]
Environmental monitoring	Measuring toxic metals in water, soils and air analysis	[7, 13, 15, 26, 27, 28, 29, 30, 31, 32]
Food safety	Water quality and beverage quality	[21, 29]
	Food analysis	[7, 21, 27, 33, 34]

METHOD OF PRINTING

This action changes particular regions or boundary of paper from being hydrophilic to hydrophobic. The two parallel hydrophobic boundary work as channels, this is due to hydrophilic sample solution cannot pass through the hydrophobic boundary or wall. As a result, the liquid runs in the channel due to capillary action[1].

All in all this method can be divided into nine techniques included inkjet printing, wax printing, photolithography, flexographic printing, plasma treatment, laser treatment, wet etching, screen printing and wax screen printing.

Inkjet Printing

Basically, inkjet technology is distributed into two main classes which is drop-on-demand (DOD) and continuous inkjet (CIJ)[35]. Yamada et al. (2015) stated that the entire typical desktop printer and all laboratory-relevant inkjet printing system depend on DOD technology. DOD technology is different from CIJ mechanism in term of continuous removal of fluid because the jetting of ink onto the substrate only take place when it is necessary as denoted by the term “drop-on-demand”. DOD inkjet printing is subdivided into four modes of actuation. The first one is piezoelectric follows by thermal, electrostatic and acoustic [35].

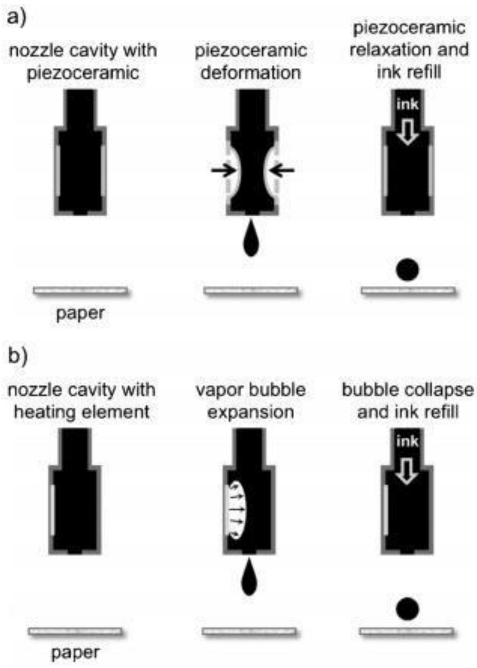

Figure 2.2 : The working principle of drop on demand (DOD) inkjet printing: a) piezoelectric inkjet and b) thermal inkjet[35].

This technique includes the paper sizing chemistry with digital inkjet printing technique. The inkjet printing can transport biomolecules and indicator reagents with accuracy into the microfluidic patterns forming biological or chemical sensing zones in the pattern and also perfect sensing tools. The possibility for merging paper sizing chemistry and inkjet printing to fabricate μPADs has verified to be of low cost and commercial volume.

Wax Printing

One of the simple fabrication technique is wax patterning method. This method included printing and baking. Besides, this method does not required a long time to be competed it only need 5-10 minutes. Wax printing is inexpensive due to wax and paper are economical and easily obtained. Other than that, this method is environmentally friendly which does not use organic solvents throughout the fabrication technique[1].

Basically, paper and wax are easily be disposed of by burning[36]. A few number of steps is involved in wax printing as it is convenient for fabricating large number which higher than 100 of μPADs in a single batch. The wax based micro patterning technology therefore is very useful for prototyping μPADs to implement low cost bioassay in low resources area.

Wax patterning has been introduced by three different ways. The first way is painting with a wax pen followed by printing with a normal inkjet printer keep on with tracing by painting with a wax pen and lastly a direct printing through a wax printer. The printing process is easy to conduct and can be completed within

5-10 minutes without the use of hygienic room, ultraviolet (UV) lamp and organic solvent [1].

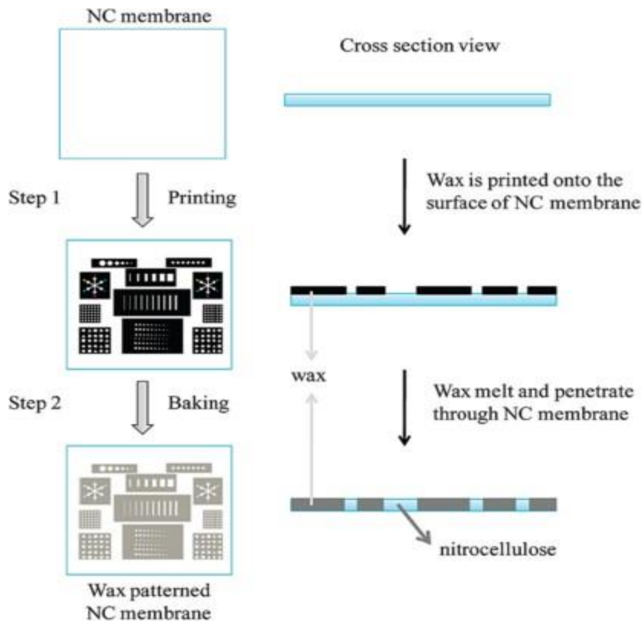

Figure 2.3: Schematic illustration of wax printing technique for fabrication of μPADs[1]

Figure 2.3 describe the schematic illustration of wax printing for fabrication of μPADs. This technique primarily consists of two steps. The first step is printing the wax pattern onto the surface of nitrocellulose membrane (NC membrane) by using a wax printer. After the completion of the printing, the wax printed NC membrane is baked in an oven of 125ºC for 5 minutes for the wax to be melt and fully pass through the membrane.

Plasma Treatment

Xia et al. (2016) proclaim that production of μPADs using plasma treatment is done by a few steps. Firstly, paper is hydrophobized via octadecyltrichlorosilane (OTS) silanization followed by regionally selected OTS silanized paper and plasma treated through a mask with channel network. The plasma uncover area of the paper is transformed to hydrophilic channel network as a result of degradation of hydrophobic OTS molecules coupled to the paper cellulose fibers before.

Some researchers stated that the paper devices produced from the plasma treatment have a benefit over the barrier design in that simple working element, such as switches, filters and separators can easily be establish into the microfluidic system [1].

Laser Treatment

A laser based production process can effectively guided the flows of fluid and ensured containment of fluids in wells by employing polymerization of a photopolymer. Xia et al., (2016) obtained the minimum width of hydrophobic barriers with the value of 120µm whereas the smallest width accounted so far for the µPADs is 80µm [1].

Moreover, the CO_2 laser which is a versatile method (allows for controlled through cutting ablative engraving of substrate) involves only one operation for cutting a piece of paper according to predesigned pattern and also can selectively modify the surface structure and property of several papers. Furthermore, the lasers system can cut various components that are beneficial in the production µPADs such as cellulose wicking pads, glass fiber source pads and Mylar-based substrates for the device housing [1].

Wet Etching

Xia et al. (2016) mentioned that this method consists of two steps where the first step involves hydrophilic filter paper which is hydrophobically patterned using trimethoxyoctadecylsilane solution as the patterning agent.

Next, this hydrophobic filter paper is contacted with a paper mask (permeate with NaOH solution consist of 30% glycerol) which allow the etching of the silanized filter paper through the etching reagent. Consequently, the masked area becomes highly hydrophilic where reservoirs and detection zones are thus developed and surrounded by the hydrophobic barriers (the unmasked area) [1].

Screen Printing

Screen printing is defined as carbon electrodes screen-printed straightly on cellulose paper to operate bipolar electrochemistry where at the same time an array of 18 screen-printed bipolar electrodes can be controlled employing a single pair of driving electrodes. Electro-generated CL is used to read out electrochemical state of the bipolar electrodes which highlight the usefulness of the coupling bipolar electrochemistry for the µPADs to operate highly multiplexed and low-cost measurement [37].

Wax Screen Printing

Figure 2.4 shows the process of wax screen printing employing two simple steps. Firstly, a simple screen-printing method and typical household supplies is used to pattern solid wax on the surface of paper. Then, hot plate is employed to melt wax into the paper to form complete hydrophobic walls. The final widths of the hydrophobic barrier is in the range of 1200-1800 mm and hydrophilic channel is in the range of 550-1000 mm at the optimal melting temperature and time [38].

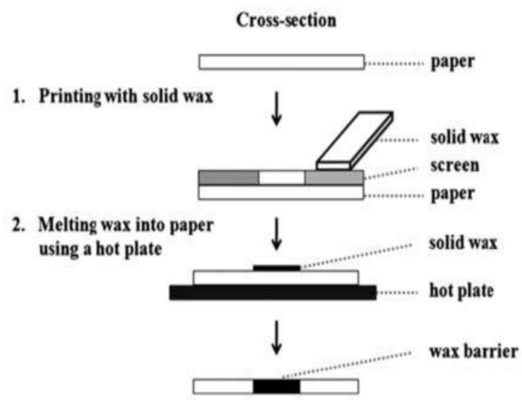

Figure 2.4: Schematic diagram of wax screen printing technique for fabrication of μPADs[1]

A wax printer is necessary for conventional wax printing. However, printing screens are inexpensive and can easily be purchased from around the globe. In addition, the wax is economical and can be purchased anywhere in the world as well environmentally friendly. Lastly, Dungchai et al. (2010) claimed that this method provide more benefits compared to other methods because it is required only a common hot plate and common printing screen that can be produced anywhere in the world, creating it ideal for production of the μPADs in emerging countries.

Photolithography

Production of the paper based plates by patterning sheets of paper into hydrophilic zones bounded by hydrophobic barriers. This method can use low cost formulation photo resistant that permits fast prototyping of paper based plates which around 15 minutes. Xia et al. (2016) proclaim that one of the publications evaluated a unique and performed fabrication method for the μPADs by using flash foam stamp lithography and compared it to common fabrication methods, for example wax printing and inkjet printing. This publication revealed that the lithography method is convenient, low cost and fast.

Dungchai et al. (2010) described that photo lithographically is a channel that display high background whereas wax printed channels display very low background[38]. This method required organic solvents, expensive photoresist and photolithography equipment.

Another method that was stated by Martinez et al. (2008) is Fast Lithographic Activation of Sheets. This method is a quick technique for laboratory prototyping of μPADs on paper. It is based on photolithography however requires a UV lamp and hotplate. The patterning can be carry out in sunlight when the UV lamp and hotplate are absent or no uncontaminated room and special facilities is required.

Fabrication of 3D μPADs

Martinez et al. (2008) described that 3D μPADs deliver fluids both vertically and laterally besides they enable streams of fluid to cross one another without mixing. According to some researcher, 3D μPADs are produced by piling alternating layers of paper and water-impermeable double sided adhesive tape, both patterns in way that channel the flow of fluid within and between layers of paper[39].

The hydrophobic polymer patterned into the paper demarcates the channel through which the fluids move laterally and the layer of water impermeable double sided tape separates the channel in neighboring layers of paper. The holes cut into the tape and allow fluids to flow vertically. The layer in the μPADs can be made by using different papers and multiple functionalities provided by the different types of paper.

DETECTION METHOD

Detection of Metal Ions

In recent times, Sriram et al. (2017) stated that some researcher used a filter paper of thickness 180 μm to fabricate μPADs via wax printing for colorimetric detection of total chromium (Cr^{3+} ions) from bag house samples[26]. The Cr^{3+} ions are toxic and dangerous to humans. Thus, the detection of Cr^{3+} ions through colorimetric using μPADs is crucial. Originally, bag house dust sample contain of metal was suspended in a 10 mm air filter punch of mixed cellulose ester (MCE) and on the detection zone of μPADs a filter was installed. Next, PDMS lid with four detection holes and one sample reservoir hole of diameter 5 and 2 mm respectively were installed on a filter sample alongside μPADs. For the elution of metal ions to the detection zones, acetate buffer solution was added via reservoir hole[26]. As a result, the color changes was seen not beyond 10 min. Tetravalent cerium (Ce^{4+}) was treated with chromium in pre-treatment zone to oxidize chromium to Cr^{6+} which reacts with 1,5-diphenylcarbazide (1,5-DPC) to form 1,5-diphenylcarbazone and Cr^{3+}[26].The presence of purple color confirms the presence of Cr^{3+} ions in the samples[26].

In addition, Chaiyo et al. (2016) developed a μPADs using filter paper with thickness 180 μm by using wax printing for colorimetric detection and electrochemical of Cu^{2+}, Cd^{2+}, and Pb^{2+}[39]. Catalytic etching of silver nanoplates (AgNPls) by thiosulphate ($S_2O_3^{2-}$) will be added at the detection zone for colorimetric detection. The color of the zone was changed from pinkish-violet to colorless when Cu^{2+} was added at detection zone[39]. The mechanism involve in this detection is as follows: When Cu2+ is presence, the preloaded Ag nanoparticles, were etched by the appearance of thiosulphate which were fragmented into smaller particles due to oxidation[39]. Thus, there was a color change from pinkish-violet to colourless.

Furthermore, Satarpai et al. (2016) produced μPADs via ink-jet printing for colorimetric detection of Pb^{2+} ion from water samples[40]. In this research, zirconium silicate acts as an adsorbent material and sodium rhodizonate (NaR) as a chromogenic agent for Pb^{2+} ions. Just as the detection zone come in contact with Pb^{2+} ions, there is a colour change from orange-brown to pink, which verify the existence of Pb^{2+}[40].

FUTURE WORK

Deinking process of waste paper

Sample collection

The methodology will be initiated with the collection of sample which is the A4 waste paper.

Impregnation

This step will be focused on the impregnation of A4 waste paper to a solution of anionic surfactant (polyethylene oxide) diluted in hot tap water in order to cause swelling of fibres and as a consequence to enhance the pulping process. More precisely, the prepared waste paper will be cut into small pieces by hand (approximately 2 cm x 2 cm). Next, about 100 g of the prepared dry samples will be added into a plastic container consists of polyethylene oxide.

The concentration of final mixture will be 15% w/w. Hot tap water with temperature of 40ºC will be used for dilution. The soaked waste paper will be mixed with the help of a stainless steel rod and will be allowed to stand for 10 minutes at 40ºC in a waterbath.

Repulping

After the completion of impregnation process, repulping of the waste paper slurry will be carried out. Repulping process aims at the detachment and separation of ink from fibres and will be conducted in a laboratory pulper.

The slurry will be added into laboratory pulper, where it will be pulped for 20 minutes under constant temperature. The initial pH of the pulp will be recorded and will also be monitored during repulping process.

Enzymatic treatment

The deinking process of waste paper will be conducted using enzyme treatment unit. Enzyme treatment unit consist of a container equipped with a stirrer, an electric heater with a thertmostat, a pH meter and thermometer.

Pulp produced from the repulping process will be diluted and transferred to the enzyme treatment unit. The enzyme treatment unit consists of a container equipped with a stirrer, an electric heater with a thertmostat, a pH meter and thermometer. Stirring was applied in order to achieve homogeneity of the mixture while through temperature control the application of optimum temperature for each enzyme preparation will be ensured. Nitric acid will be used for pH adjustment.

Upon achieving optimum temperature and pH conditions, the enzymes were diluted in 500 mL of water and finally added to the pulp. The added amount of each enzyme preparation will be corresponding to 150 FPU/100 g paper. This process will take about 20 minutes. The process will be terminated with the inactivation of the enzyme by pH change, through addition of sodium hydroxide (NaOH) in order to adjust pH about 11.

Papermaking

The handsheets will be prepared using a laboratory sheet press. The handsheets will be air dried for 24 hours at room temperature.

Fabrication of μPADs

The fabrication of μPADs will be conducted by using a wax printer for printing the wax pattern on the paper. A hot plate will be used for wax melting.

The design of the wax-pattern will be drawn on waste paper including the colorimetric detection zone with a cycle shape and diameter 3 mm. The wax-pattern will be printed using a solid wax printer.

After printing the wax-pattern, the printed paper will be placed on a hot plate and the wax on the waste paper will be melted and spread throughout the thickness of the paper. The area that will be covered with the wax is hydrophobic and the area without the wax is a hydrophilic. Figure 2.5 shows the pattern that will be used in fabrication of μPADs

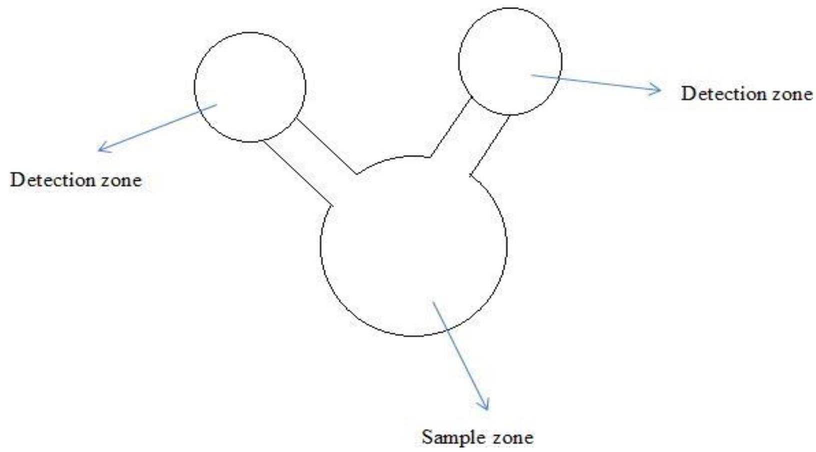

Figure 2.5: Schematic diagram patterned for fabrication of μPADs

Testable of μPADs

After the fabrication of μPADs, the testable of these devices will be conducted through colorimetric detection method. This colorimetric detection will be focused on the detection of heavy metals from water sample. The nanoparticles that will be used is zirconium silicate that act as an adsorbent material and sodium rhodizonate(NaR) that act as chromogenic agent for detection of Pb^{2+} ions.

Firstly, the adsorbent material will be coated on to the detection zone of μPADs followed by NaR. The same principle also will be applied to detection of Cu metals but bathocuproine will be used as chromogenic agent.

CONCLUSION

The increase in the number and improved quality of the articles published on μPADs has shown that μPADs has been gaining so much attention. μPADs technology are improving to meet the consumer and industrial condition, thus, paper is the most ideal material that fulfill all the requirement needed for changeover of this technology from research laboratory to the industrial commercialisation.

The utilization of waste paper as the material of μPADs, provides a simple, economical and easily operated by the users which permit a convenient analytical platform to be benefits human being in a variety of applications. The applications of μPADs are rising following the time due to its abilities in preparation, detection and flow control.

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