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Advances on paper-based analytical devices (μPADs) – literature review

Abstract: *Microfluidic paper-based analytical devices (μPADs) are relatively new group of analytical tools. Work principles of such devices partially evolved from chromatographic techniques, particularly planar chromatography. Recently, analytical devices based on paper are subject of extensive research, mostly focused on fast and non-expensive biochemical analysis but also for screening of medical and environmental samples. Attempts are being made for their applications in forensic - to organic explosives detection and in medicine - to diseases diagnosis. In this short review we presented a recent advances in area of μPADs technology.*

Key Words: *Microfluidic paper-based analytical devices (μPADs); qualitative analysis, quantitative analysis, medical and biochemical analysis, environmental screening, analytical chemistry.*

1. Introduction

Laboratories on a chip (lab-on-chip or LOC) – microfluidic analytical devices - are subject of extensive research over last twenty years. Through them new ways in medicine, biochemistry, genetic, cell biology can be opened. Simple and robust manipulation of small volumes of fluids within microchannels has been regarded as the most important advantage of laboratories on a chip [1]. Especially important for their application are the benefits flowing of low consumption of reagents and analytes [2]. LOC are used in a wide range of practical applications, particularly in the biomedical sciences and environmental studies, also in biochemistry. They are recognized as the convenient tools for detection and determination of many inorganic and organic compounds. Moreover, they provide number of analytical and diagnostic capabilities, which may revolutionize medicine and the pharmaceutical industry. In recent times labs-on-chip are successfully used in clinical analysis of blood [3, 4], detection of proteins and pathogens [5-7], environmental pollutants [8, 9], genetic studies [10, 11] and the pharmaceutical industry [12, 13]. Miniaturized medical diagnostics devices can be important for people living in developing countries, where access to laboratories or diagnostic equipment is difficult or even impossible [1].

2. Characterization of „lab-on-chip”

Considering construction and manufacturing techniques of the microfluidic devices, we may distinguish two main groups of laboratories on a chip. The first one gather devices known as μTAS (micro total analysis systems) that are created on the basis of glass, quartz, silicon and polymers and combined with external units (such as samplers, detectors, electronic units), in which fluid flow is controlled by pumps and valves [1]. It is assumed, that the first device constructed from glass and silicon was developed in 1975 [14, 15]. Interestingly, it was based on gas chromatography principles. Currently, materials and manufacturing techniques of μTAS, as well as their application range have been greatly improved and expanded, which is widely described in the scientific literature. From the other side, since year 2008, we may observe rapid development of another group of microfluidic analytical devices, where the major part of the construction is based on a paper material (cellulose) - and hence known as μPADs (paper-based microfluidic analytical devices) (Fig. 1). This type includes non-expensive and easy to make paper chips, which can be considered as fully equipped laboratory instruments. They are designed to perform specific tasks, mainly in order to detect different types of substances [16]. In such devices the fluid flow is caused by capillary forces, which controlling is currently under extensive investigation [17].

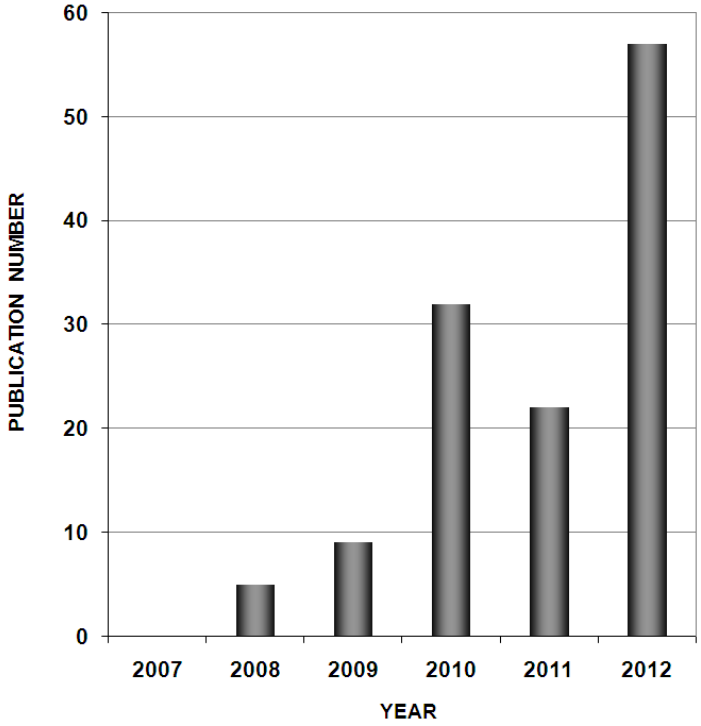

Fig. 1. Research papers concerning μPADs in years 2007-12 (source: Web of Knowledge; data: 15.01.2103; key word: paper-based microfluidic devices).

3. μPADs - materials and manufacturing techniques

The main goal of manufacturing a μPADs is to create hydrophobic barriers, which are directing fluid flow through microchannels within the base material (paper). The first microfluidic device based on paper (with the exception of paper strips to pH determination) was invented and described by Whiteside Group at Harvard University in 2007 [18]. Photolithography technique to made microtunnels was performed using a photoresist polymer and chromatography paper. This device was used for glucose and protein determination in the urine. It is noteworthy to say that μPADs production is possible even in home using adhesive tape and paper [19].

Currently, the scientific publications describe a number of techniques and materials used to form hydrophobic barriers, both on the typical filter or chromatographic paper. They involve polymers (such as SU-8 photoresist, AKD (alkyl ketene dimer), PMMA (poly(methyl methacrylate), PDMS (polydimethylsiloxane), PS (polystyrene)) used in the photolithographic technique [18] and their solutions used in converted ink plotters [20] and typical ink jet printers [21]. Next group of materials consist a waxes used for commercial printing [22, 23] and screen-printing [24]. μPADs can be also created by using flexographic printing [25], a laser [26] and plasma treatment [27] and finally - by cutting knives [28, 29].

4. μPADs - typical applications

Today, we may observe an increase of interest in new strategies allowing to rapid analysis and diagnostics for clinical, environmental and forensic purposes without sophisticated instrumentation. According to literature data, application of paper systematically increase, as can be seen from the graph presented in Figure 1. In laboratories, paper is commonly used as basic material for filtration and chromatography. Typical μPADs detection systems are based on colorimetry, electrochemistry, chemiluminescence and electrochemiluminescence, however colorimetric and electrochemical qualitative and quantitative determinations are the most popular [16]. The first diagnostic system involving paper based device was used for colorimetric determination of glucose and protein in urine [18]. Brennan's research team developed a device, which allow to perform a rapid (in few minutes) detection of paraoxon and aflatoxin B1 at concentrations~ 100 nM and ~ 30 nM, respectively [30]. μPADs are used in environmental studies for heavy metals determination (Pb and Cd) [31], in clinical analysis of blood [32-34] and genetic for DNA detection [35, 36], also in food quality control [37, 38]. Attempts are being made for their applications in forensic - to organic explosives detection [39] and in medicine - to diseases diagnosis [40]. Numbers of research teams are extensively working on application of μPADs in telemedicine services as well as its hyphenation with the external devices [41-43].

5. Conclusions

Research concerning μPADs is carried out for last few years. However, as it is presented in this survey, the usage of paper as the base material for analytical and diagnostic purposes is in the center of interest of many researchers in the world. It is obvious that μPADs cannot replace sophisticated laboratory equipment, including spectrometers or chromatographs, which is used in laboratories around the world. However, in specific situations, especially in developing countries, μPADs may be a very good alternative, when access to hi-tech equipment is very limited. This becomes even more real, when such methodology will be included in the

scope of telemedicine services. Under such conditions, μPADs photo taken by mobile phone can be instantly transferred thousands miles away from analysis place to specialized laboratory.

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