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Point of care testing: The impact of nanotechnology

Leila Syedmoradi [a,b,1], Maryam Daneshpour [a,c,1], Mehrdad Alvandipour [a,1], Frank A. Gomez [d], Hassan Hajghassem [e], Kobra Omidfar [a,f,*]

[a] Biosensor Research Center, Endocrinology and Metabolism Molecular–Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Medical Nanotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran
[c] Biotechnology Department, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[d] Department of Chemistry and Biochemistry, California State University, Los Angeles, 5151 State University, Drive, Los Angeles, CA, 90032-8202 USA
[e] Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran
[f] Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Point-of-care (POC) diagnostic devices are integral in the health care system and particularly for the diagnosis and monitoring of diseases. POC testing has a variety of advantages including the ability to provide rapid and accurate results, ease of use, low cost, and little need for specialized equipment. One of the goals of POC testing is the development of a chip-based, miniaturized, portable, and self-containing system that allows for the assay of different analytes in complex samples. To achieve these goals, many researchers have focused on paper-based and printed electrode technologies as the material for fabricating POC diagnostic systems. These technologies are affordable, sensitive, user-friendly, rapid, and scalable for manufacturing. Moreover, the combination such devices with nanomaterials provide a path for the development of highly sensitive and selective biosensors for future generation POC tools.

This review article discusses present technologies in on-site or at home POC diagnostic assays implemented in paper-based microfluidic and screen printing devices over the past decade as well as in the near future. In addition, recent advances in the application of nanomaterials such as gold nanoparticles, carbon nanotubes (CNTs), magnetic nanoparticles, and graphene in POC devices will be reviewed. The factors that limit POC testing to become real world products and future directions are also identified.

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* Corresponding author at: Biosensor Research Center, Endocrinology and Metabolism Cellular and Molecular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran, P.O. Box 14395/1179, Tehran, Iran.
E-mail address: omidfar@tums.ac.ir (K. Omidfar).
[1] Equal contributors.

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1. Introduction

Major advances in healthcare system and analytical process have been focused on developing portable, reusable, and effective miniaturized platform or point-of-care (POC) systems. POC devices assume that all tests can be at or near the site of patient care. (McPartlin and O'Kennedy, 2014; Omidfar et al., 2012a; Tang et al., 2016). POC testing is a paradigm shift from traditional diagnostic tests in the clinical laboratory setting to near-patient settings, providing physicians with timely diagnostic information enabling better informed decisions regarding diagnosis and treatment (Gomez, 2013).

The guidelines generally required for developing efficient POC devices are provided by the World Health Organization (WHO). These guidelines are known as ASSURED, in which the acronym ASSURED stands for affordable, sensitive, specific, user-friendly, rapid/robust, equipment-free or minimal, and delivered to the greatest need (Mabey et al., 2004).

POC devices can be divided into two classes including small hand-held and larger bench-top devices. Small hand-held devices are developed using state-of-the-art microfabrication techniques, which automate sample preparation, assay steps, analysis and detection of signals (Srinivasan and Tung, 2015; St John and Price, 2014). These devices offer qualitative or quantitative measurement of a wide range of analytes. Larger bench-top devices are essentially miniaturized versions of mainframe central lab equipments which have been reduced in both size and complexity.

Various reports are available to document the growth in vitro diagnostics (IVD) markets including various categories such as POC testing. The global POC diagnostics market is expected to reach USD 27.5 billion by 2018 at an estimated compound annual growth rate (CAGR) of 9.3% from 2013 to 2018 (marketsandmarkets.com; Report Code: MD 2702) (Sharma et al., 2015). LFAs constitute the majority of the POC diagnostics market. Globally, more than 100 companies are producing a wide range of LF tests. The integration of molecular diagnostics with POC testing is the fastest growing area in recent years. The total molecular diagnostics market is estimated to grow and reach USD 9333.8 million by 2020. The molecular diagnostics market, by application, is categorized into infectious diseases, oncology, genetics, blood screening, microbiology, and others (cardiovascular diseases, neurological diseases, DNA fingerprinting, tissue typing, and food pathogen detection testing).

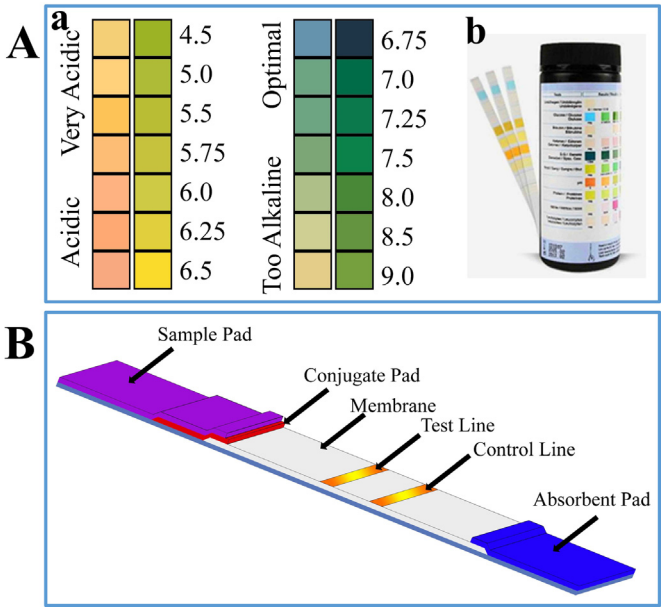

Fig. 1. Paper-based diagnostic platforms: (A) dipsticks, including (a) diagnostic pH test strips and (b) urine test strips. (B) Schematic view of a typical lateral flow test strip, including sample pad, conjugate pad, incubation and detection zone with test and control lines and final absorbent pad.

Herein, we restrict our discussion to two categories including paper-based microfluidic and printed electrodes (PE) POC diagnostic devices. Then we offer an authoritative review on the impact of nanotechnology based POC systems in the recent years to summarize and comment on their development and advances. In particular, carbon nanotubes, graphene and metal nanoparticles as well as their corresponding nanocomposites will be discussed. Finally, the future perspectives, opportunities and challenges in this field will be discussed.

2. POC testing

In the following sub-sections, POC testing based on paper-based microfluidic and printed electrodes are presented.

2.1. Strip-based POC assays: capillary flow tests

2.1.1. Dipsticks

Paper-based analytical devices (Fig. 1A), in the form of paper-based indicators and dipstick assays, have been used for rapid detection of a wide range of analytes due to simple design, easy to manufacture and convenient to use.

The first paper-based diabetes dipstick test was established in the 1950s to determine the level of glucose in urine specimens. Nowadays, standard urine test strips have been employed to detect metabolic products (e.g., protein, glucose, and salt) from patients with nephritic or diabetic diseases (Liana et al., 2012; Park et al., 2016).

2.1.2. Lateral flow tests

The capillary flow platform, also known as LFA or test strip, is a promising tool for the identification of analytes and pathogens at the POC and/or home use. This sensing platform offers an inexpensive, relatively rapid assay, and ability to operate by minimally trained personnel in regions where no sophisticated laboratory facilities are available. In LFA, the liquid sample moves along a solid paper-based membrane through capillary forces without any applied pressure which is controlled by the wettability and characteristic sizes of porous substrate.

These types of assays require small quantities of liquid sample and time of 5–15 min for detecting the presence/absence of analyte in the specimen (Li and Macdonald, 2016; Omidfar et al., 2013; Park et al., 2016; Yamada et al., 2015). LF immunoassays as are among the most commercially successful microfluidic POC devices (Omidfar et al., 2013; Posthuma-Trumpie et al., 2009; Zhou et al., 2015). When an antibody and its fragments are employed as bioreceptors, this test is called a "lateral flow immunoassay" (LFIA)