Development of Glucometer-assisted Nano Immunoassay for the Detection of Creatinine

Zein Barakat
University of South Florida, USA

Abstract:

This study investigates a one-step reaction strategy for quantifying creatinine via an enzymatic activity using a personal glucose meter (PGM). Creatinine is a waste product that is filtered through the kidneys. To be able to detect creatinine levels at an early stage, allows for an early diagnosis of kidney malfunction. Easy and noninvasive detection of creatinine in urine is diagnostically favorable. A PGM is commercially available; however, it can only detect a single target, glucose. A link between the functionality of a PGM, an enzymatic reaction, and a specific antibody-target interaction could enable the quantification of non-glucose targets. Invertase is one enzyme that catalyzes the breakdown of sucrose into glucose and fructose, and it can form a link between the detection of glucose and non-glucose targets. The proposed detection scheme uses the conventional PGM without changing its design. Two types of immunoassays, competitive and sandwich, were developed and their ability to sensitively and specifically detect creatinine was compared. Two nanocomposites are constructed to develop the immunoassays. To begin with, one nanocomposite was made up of iron oxide magnetic nanoparticles (IOMNP), poly(diallyldimethylammonium) (PDDA), gold nanoparticles (AuNPs), and creatinine primary antibody (Ab1). The second nanocomposite was made up of graphene oxide (GO), PDDA, AuNPs, creatinine secondary antibody (Ab2), and invertase. The competitive immunoassay showed higher sensitivity to creatinine within the human range. With further development, this device can be easily utilized in neighborhood clinics, or at home, instead of a hospital or a centralized lab. It offers a combination of ease of operation and quantification that may be particularly useful in environments that lack refrigeration, electricity, and other resources, such as remote villages in the developing world.

Recent advances in mobile network and smartphones have provided an enormous opportunity for transforming in vitro diagnostics (IVD) from central labs to home or other points of care (POC). A major challenge to achieving the goal is a long time and high costs associated with developing POC IVD devices in mobile Health (mHealth). Instead of developing a new POC device for every new IVD target, we and others are taking advantage of decades of research, development, engineering and continuous improvement of the blood glucose meter (BGM), including those already integrated with smartphones, and transforming the BGM into a general healthcare meter for POC IVDs of a wide range of biomarkers, therapeutic drugs and other analytical targets. In this review, we summarize methods to transduce and amplify selective binding of targets by antibodies, DNA/RNA aptamers, DNAzyme/ribozymes and protein enzymes into signals such as glucose or NADH that can be measured by commercially available BGM, making it possible to adapt many clinical assays performed in central labs, such as immunoassays, aptamer/DNAzyme assays, molecular diagnostic assays, and enzymatic activity assays onto BGM platform for quantification of non-glucose targets for a wide variety of IVDs in mHealth.

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