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A smartphone metabolomics platform and its application to the assessment of cisplatin-induced kidney toxicity

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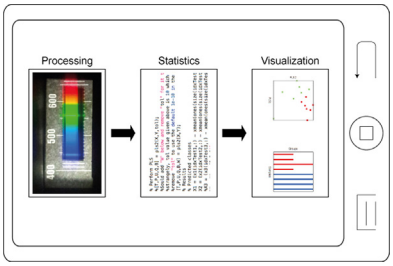
HIGHLIGHTS

- We established a portable metabolomics platform using a smartphone.
- It included all the steps of acquisition, processing, analysis, and visualization.
- All the software parts were built using freely available applications.
- Cisplatin toxicity was evaluated using the smartphone metabolomics.

GRAPHICAL ABSTRACT



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ABSTRACT

The application of smartphones to medical devices has been gaining attention in addressing accessibility and cost issues in healthcare, and the detection of medically relevant compounds has been demonstrated using customized smartphone hardware and/or software. Metabolomics, a newly rising omics field, has also spawned many medical applications but requires highly sophisticated and expensive equipment. Here, we describe a portable smartphone platform, built with readily available and affordable materials, that can perform all of the critical aspects of metabolomics. Excluding the smartphone itself, the total materials for the platform were obtained at less than US $20. For spectral data acquisition, the system utilized visible light (400–700 nm) and a built-in camera. All of the data processing, statistical analysis, and final-visualization components necessary for decision making were implemented in the smartphone platform. The platform is generally applicable as long as the analytes absorb visible light. We provide a proof-of-concept example wherein the metabolomics platform was applied to the assessment of cisplatin-induced kidney toxicity in a rat model, correctly predicting 7 out of 8 test samples.

1. Introduction

In many regions of the world, access to healthcare is limited due to insufficient medical infrastructure or limited availability of medical devices [1,2]. Recent cell phones, especially smartphones, are equipped with various sensors and powerful processors; as such, they offer effective functionalities as platforms for data acquisition and analysis. Therefore, the use of smartphones as potential medical devices is a promising means of addressing the growing needs for cost efficiency and easy accessibility in healthcare [3–5]. Actually, smartphones, incorporated with extra devices, have been demonstrated to function as a microscope [6,7], a fluorescence detecting device [8], and a spectrometer [9]. Still, in many of these cases, smartphones are used mainly for data acquisition or simple visualization, whereas data processing, analysis and final interpretation are performed with separate,

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"real" computers. This separate-device requirement can limit the portability of potential smartphone-derived medical devices to the point of care. Others also reported the application of smartphones to the analysis of pre-defined substances such as cholesterol, vitamin D, proton ion, and those specified on urine dipsticks [10–14]. Although they are stand-alone applications that do not require separate computers, they are limited to the particular purpose(s) specified in the studies. For example, the hardware and sample preparation for the vitamin D detection are quite different from those for the detection of cholesterol [10,12]. Modifications in hardware or software are required for the above methods to be used for the detection of other materials or the monitoring of other health conditions. In this regard, a general-purpose smartphone platform that can perform stand-alone "metabolomics" analysis and is not limited to particular analytes may have merits [15].

Metabolomics is a newly emerging omics approach to the investigation of metabolic phenotype changes induced by environmental or endogenous factors [16]. It has shown promising results in healthcare fields, especially in disease diagnosis and drug-toxicity assessment, as reviewed recently [17–21]. In drug-toxicity assessment, metabolomics is often concerned with finding toxicity-related biomarkers by investigating the changes in metabolic signatures induced by drug exposure. For example, potentially useful drug-toxicity biomarkers have been reported for major organs such as liver and kidney [22–25] or for systemic toxicity [26]. Toxicity-related biomarkers can be especially useful for non-invasive toxicity assessment or prediction of drug-induced toxicity before administration of drugs. These potential applications of metabolomics to toxicology have inspired the coining of the terms toxico-metabolomics or pharmacometabol(n)omics [27–29].

In modern metabolomics studies, metabolic profiles have been analyzed primarily by mass spectrometry (MS) or NMR spectroscopy. The advantages of these techniques include detailed information on molecular structures, high-precision detection of metabolic signatures, and large dynamic ranges in quantification [30,31]. Although they undoubtedly have made essential contributions to the very establishment of the metabolomics field, they require highly sophisticated and high-cost hardware that is not always available [32–34]. The underlying theories and technical aspects of these approaches are also highly sophisticated, and familiarization with them requires extensive knowledge and experience. In general, these factors limit the accessibility of these techniques in impoverished regions or at the point of care [35–38].

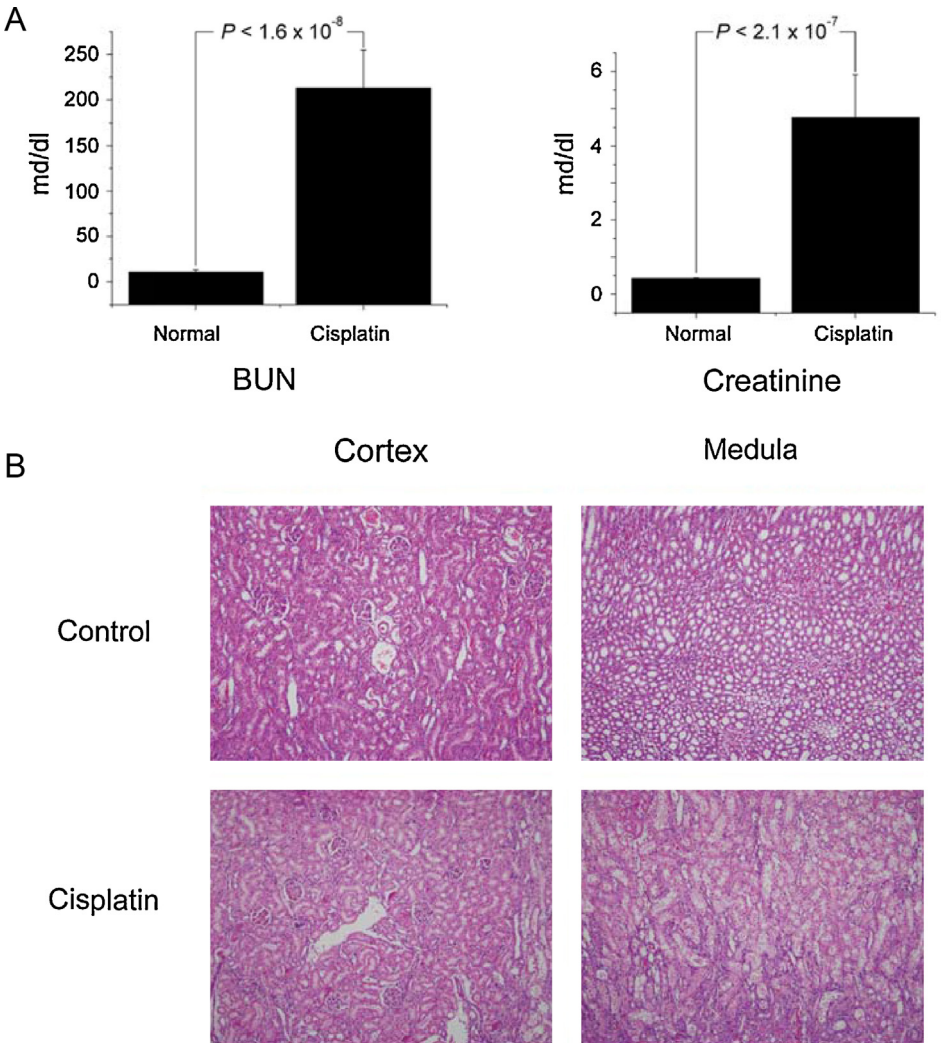

Fig. 1. Hematological and histological effects of cisplatin treatment on kidney.
Blood and kidney samples obtained from animals administered saline (control) or 10 mg/kg cisplatin (cisplatin) were analyzed. (A) Hematological BUN and Cr level differences. The mean, standard deviation, and associated *p*-values obtained by student's *t*-test are indicated. (B) Cisplatin-induced kidney toxicity as evaluated by H&E staining. The first row shows the control group and the second row the cisplatin group.