Journal of Pharmaceutical Analysis 15 (2025) 101041

Contents lists available at ScienceDirect

Journal of Pharmaceutical Analysis

journal homepage: www.elsevier.com/locate/jpa

Original article

Development of a smartphone-integrated handheld automated biochemical analyzer for point-of-care testing of urinary albumin

Ze Wu [a, 1], Peng Zhang [a, 1], Wei Xiao [b, 1], Qian Chen [c], Wangrun Lin [a], Peipei Chen [a, d], Kangwei Chen [a], Qiangqiang Fu [a, ***], Zhijian Wang [c, **], Lei Zheng [a, *]

[a] Department of Laboratory Medicine, Nanfang Hospital, Southern Medical University, Guangzhou, 510515, China
[b] Department of Laboratory Medicine, Guangdong Second Provincial General Hospital, Guangzhou, 510320, China
[c] Department of Obstetrics and Gynaecology, Nanfang Hospital, Southern Medical University, Guangzhou, 510515, China
[d] Department of Laboratory Medicine, Foshan Maternal and Child Health Hospital, Foshan, Guangdong, 528000, China

ARTICLE INFO

Article history:
Received 1 April 2024
Received in revised form
26 June 2024
Accepted 9 July 2024
Available online 14 July 2024

Keywords:
Chronic kidney disease
Albumin
Smartphone
Biochemical analyzer
Point-of-care testing

ABSTRACT

The level of urinary albumin is a critical indicator for the early diagnosis and management of chronic kidney disease (CKD). However, existing methods for detecting albumin are not conducive to point-of-care testing due to the complexity of reagent addition and incubation processes. This study presents a smartphone-integrated handheld automated biochemical analyzer (sHABA) designed for point-of-care testing of urinary albumin. The sHABA features a pre-loaded, disposable reagent cassette with reagents for the albumin assay arranged in the order of their addition within a hose. The smartphone-integrated analyzer can drive the reagents following a preset program, to enable automatic sequential addition. The sHABA has a detection limit for albumin of 5.9 mg/L and a linear detection range from 7 to 450 mg/L. The consistency of albumin level detection in 931 urine samples using sHABA with clinical tests indicates good sensitivity (95.78%) and specificity (90.16%). This research advances the field by providing an automated detection method for albumin in a portable device, allowing even untrained individuals to monitor CKD in real time at the patient's bedside. In the context of promoting tiered diagnosis and treatment, the sHABA has the potential to become an essential tool for the early diagnosis and comprehensive management of CKD and other chronic conditions.

1. Introduction

Chronic kidney disease (CKD) is a growing global health problem, with an estimated prevalence between 10.1% and 13.3% [1–3], and is rapidly increasing, especially in remote and resource-poor areas. There are few signs or symptoms in the early stages of CKD, which makes the early diagnosis dependent on laboratory measures of kidney function [4,5]. Point-of-care testing (POCT) holds significant potential to improve health outcomes for CKD patients [6–8], especially those with comorbidities such as hypertension, hyperlipidemia, and diabetes [4,9].

Urinary albumin (ALB) is an important early indicator of renal damage in CKD patients and a key factor in the disease's development [10–14]. There are various methods to assess urinary ALB level, ranging from convenient dipstick tests [15] to more complex enzyme-linked immunosorbent assay (ELISA) [16,17] and high-performance liquid chromatography (HPLC) methods [18]. However, dipstick tests cannot quantify urinary ALB, and laboratory tests based on ELISA and HPLC are operationally complex and require large-scale equipment. These limitations often prevent patients from receiving timely and effective health management post-discharge [19]. Therefore, there is an urgent need to develop a platform that can rapidly and conveniently assay ALB levels without the need for bulky equipment and complex reagent addition. Immunoturbidimetry, especially latex-enhanced immunoturbidimetric assay, is a commonly used clinical method for detecting urinary ALB [20–22]. Latex-enhanced immunoturbidimetric detects ALB by measuring the increase in turbidity resulting from the clumping of latex particles coated with specific antibodies when they bind to the ALB in a sample. It can accurately quantify ALB in urine samples and is particularly suitable for detecting the presence of ALB during early kidney damage. Latex-enhanced immunoturbidimetric assay offers higher accuracy than most

* Corresponding author.
** Corresponding author.
*** Corresponding author.
E-mail addresses: fqq_2021@i.smu.edu.cn (Q. Fu), wzjnfyy@163.com (Z. Wang), nfyyzhenglei@smu.edu.cn (L. Zheng).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.jpha.2024.101041

currently proposed POCT methods and has lower cost and equipment requirements compared to other immunoassays and HPLC methods. Due to these advantages, POCT platforms can be developed based on the traditional latex-enhanced immunoturbidimetric assay that is more cost-effective, convenient and accurate.

In a traditional laboratory setting, immunoturbidimetric assay requires careful mixing of immunosphere and samples in a cuvette at a fixed ratio, waiting for a few minutes for the mixture to react, and then using a turbidimeter to measure the turbidity of the reaction product to assess ALB concentration. The process requires professional technicians to use pipettes for reagents addition and mixing, and expensive equipment for results reading and data analysis. To enable patient self-testing at home, manual processes of adding reagents and incubation need to be avoided. A low-cost method that automates reagent control is urgently needed [23]. In addition, solutions for reading and analyzing results that do not rely on large instruments and sites are also important for implementing POCT. With the increasing functionality and popularity of smartphones, they have become one of the best companions for developing portable POCT systems [24–26]. Therefore, a smartphone-based automated reagent control method is an ideal solution for home POCT that enables automated ALB testing.

Here, we introduced a novel smartphone-integrated handheld automated biochemistry analyzer (sHABA). In the sHABA system, the ALB detection reagents (sample diluent, latex-microspheres and buffer) were preloaded in segments within a section of hose, which was connected to a peristaltic pump at one end and led into a reaction well at the other. A smartphone could regulate the addition and cessation of reagents by indirectly controlling the voltage of the peristaltic pump through a relay switch, following a set program to turn it on or off at specific time intervals. The reagents in the hose are added sequentially to the test wells according to the set program. Additionally, the smartphone was able to automatically read the light intensity transmitted through the reaction well in the reagent cassette (Fig. 1A). In samples with low or no ALB, latex microspheres hardly aggregated (Fig. S1A), absorbing less light and allowing more to be read by the smartphone. High ALB levels triggered substantial antigen-antibody reactions, causing microsphere aggregation (Fig. S1B), increased light absorption, and reduced smartphone readings (Fig. 1A). Under the control of a set program, the voltage of the peristaltic pump shows pulsed changes. Within a cycle of these voltage changes, which includes the addition of a reagent into the detection well and incubation (Fig. 1B), the light intensity read by the smartphone changes accordingly (Fig. 1C). This portable, fast, automated biochemical testing platform enables automated on-site diagnostics in situations where workspace is limited, resources are minimal, and power supply is unreliable.

2. Materials and methods

2.1. Chemicals and materials

The ALB test kits (latex-enhanced immunoturbidimetric assay) were purchased from Huisong Technology Development Co., Ltd. (Shenzhen, China). Water-soluble blue pigment was obtained from

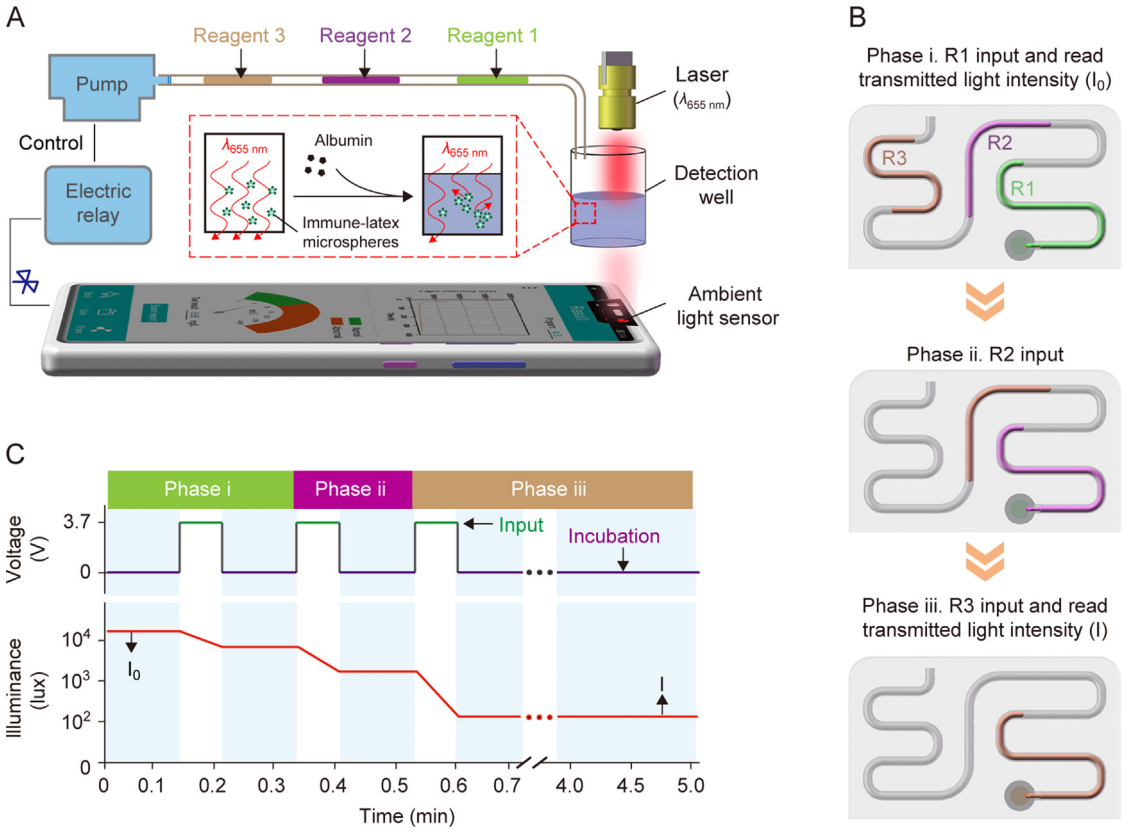

Fig. 1. Working principle of smartphone-integrated handheld automated biochemistry analyzer (sHABA). (A) schematic representation of sHABA for albumin (ALB) detection. (B) The detection reagent status in the reagent cassette at different phases. Under the control of smartphone, the peristaltic pump drives the pre-loaded detection reagents to be added to the reaction well according to the program, while recording the transmitted light signal. (C) Schematic diagram of sHABA response process. The changes in voltage on the peristaltic pump and the light intensity measured by the smartphone over time. R1: reagent 1; R2: reagent 2; R3: reagent 3.

Zhejiang Dragoni Colour Technology Co., Ltd. (Hangzhou, China). The peristaltic pump was acquired from Hangzhou Lifu Electromechanical Manufacturing Co., Ltd (Hangzhou, China). A desktop 3D printer (Whale 2) was purchased from Shenzhen Nova Intelligent Technology Co., Ltd. (Shenzhen, China). Black photosensitive resin and polylactic acid (PLA) used for fabricating the device were sourced from Shenzhen Creality 3D Technology Co., Ltd. (Shenzhen, China). Thermoplastic elastomer (TPE) hoses with an inner diameter of 2 mm and an outer diameter of 2.4 mm, along with their corresponding joints, were procured from Chengdu Zhongcheng Xinda Technology Co., Ltd. (Chengdu, China). Lasers (655 nm, 1 mW) were sourced from Shenzhen Ruixin Hengchuang Electronics Co., Ltd. (Shenzhen, China). Electric relays were custom-made by Shenzhen Yueyu Electronic Technology Co., Ltd. (Shenzhen, China). A heating film (65 mm × 35 mm × 0.2 mm) and temperature controller were purchased from Shenzhen Hongxin Electric Heating Technology Co., Ltd. (Shenzhen, China). All other electronic components were supplied by Shenzhen Weixinyuan Technology Co., Ltd. (Shenzhen, China).

2.2. Urine samples

Urine samples from healthy individuals and patients with CKD were remaining samples collected from the Laboratory Medicine Department of Nanfang Hospital (Guangzhou, China). Additionally, part of urine samples from phases CKD 3–5 were collected from the Second People's Hospital of Guangdong Province (Guangzhou, China). The levels of ALB of these urine samples were tested using the automated biochemical analyzer (BECKMAN AU5800, Beckman Coulter, Brea, CA, China). All clinical samples were collected and used with the approval of the Ethics Committee of Nanfang Hospital, Southern Medical University (Approval No.: NFEC-2023-022).

2.3. Preparation of the reagent cassette

The sHABA system comprises two components: a disposable reagent cassette and a portable smartphone-integrated analyzer. Disposable cartridges are a key feature of the platform, enabling automated reagents addition, fast turnaround times and low cost per test. A disposable reagent cassette comprises a 3D-printed body, an embedded TPE hose, and a reaction well with a glass bottom (Fig. 2A). The body of the reagent cassette was designed using SolidWorks 2020 and fabricated by 3D printing with black rigid photosensitive resin. A curved groove (semicircular arc with a diameter of 2.5 mm) was designed on the upper surface of the reagent cassette. TPE hose was embedded in the groove using adhesive. The starting end of the TPE hose was located on the front surface of the reagent cassette, and the end was connected to the reaction well. To produce a reagent cassette, test reagents were injected into the TPE hose using a pipettor from the starting end of the TPE tubing, with air between the reagents to prevent mixing. To prevent reagent mixing during transportation and storage, a cassette cover with several semicircular protrusions was designed. When the cover is tightly combined with the reagent cassette, these protrusions compress the TPE hose, creating segmented sealing and ensuring reagent stability during transportation and storage (Fig. S2). As a disposable consumable, the reagent cassette is compact and easy to store (70 mm × 42 mm × 8 mm) (Fig. 2B). The cost of the disposable kit, including the reagents inside, the 3D printing raw materials, and a hose, totals just $1.50 (Table S1), an extremely low cost that could boost its popularity in resource-poor and remote areas.

The reagent cassette used for ALB detection preloads the following reagents inside the TPE tubing: 60 μL sample diluent, 60 μL immune latex microspheres, and 60 μL buffer, with 60 μL of air spaced between each component. The reagent cassettes containing the test reagents were sealed with a cover and stored at 4 °C.

2.4. Design and fabrication of the smartphone-integrated analyzer

The smartphone-integrated analyzer is a portable device (80 mm × 70 mm × 60 mm) and is equipped with integrated electric relay, laser light sources, a 3.7 V lithium battery, peristaltic pumps, charging ports, and switch (Figs. 2C and D). The smartphone-integrated analyzer was designed using SolidWorks 2020 and manufactured through 3D printing with PLA material. The electronic components are connected according to the detailed working circuit diagram (Fig. S3). In the front of the reader, there was a rectangular opening (70 mm × 12 mm × 42 mm) for inserting the reagent cassette, with dimensions matching that of the cassette. The outlet of the peristaltic pump was connected to a steel capillary tube with an outer diameter of 2.0 mm. The smartphone connects to electric relay through bluetooth and configures the running program, which includes parameters such as the duration of each opening and closing, as well as the desired number of cycles. The total cost of the smartphone-based analyzer is about $19.7 (Table S1), making it affordable for almost every household, and the fact that it can be used anywhere without the need for other devices or external power supplies greatly enriches the application scenarios of the method.

2.5. ALB detection performance of sHABA

For ALB detecting, 2 μL of ALB standard diluted in phosphate-buffered saline (PBS) buffer was added into the reaction well of the reagent cassette. The peristaltic pump was adjusted to flow rate to 10 μL/s. The sHABA running program was set as follows: run each cycle for 6 s, stop for 10 s, and run a total of 3 cycles. Subsequently, the reagent cassette was inserted into the smartphone-integrated analyzer, and the switch was turned on, and the light intensity (I_0) was recorded. After running for 5 min, the transmitted light intensity (I) was recorded. The absorbance of ALB detection was calculated using Lambert–Beer's ($OD = \lg I_0/I$). During preliminary studies, a smartphone was used to construct the sHABA, while a free smartphone app (*phyphox*) (Fig. S4) was utilized to analyze light intensity, determining the method's feasibility and optimizing assay conditions. Subsequently, we developed a smartphone app called *sHABA* for light intensity reading and result analysis.

3. Results and discussion

3.1. Performance of sHABA

The sHABA system is an innovative smartphone-integrated biochemistry analyzer. The reagent cassette is first inserted into the analyzer and the urine sample is added to the reaction well. The smartphone then begins to control the peristaltic pump that feeds reagents from the TPE hose into the reaction well and automatically manages the reagent addition and incubation steps. For ALB testing, a urine sample is first added to the reagent cassette's reaction well and the kit is subsequently inserted into the analyzer. When the reagent cassette is inserted into the reader, the metal tube of the peristaltic pump is inserted into the entry of the reagent cassette, establishing the connection between the reagent cassette and the smartphone integrated analyzer. Subsequently, the smartphone application programs the peristaltic pump to rotate or stop for a designated duration, effectively driving the reagent from the cassette into the reaction well in a programmable manner. This process facilitates the completion of automated detection. Simultaneously, the light emitted by the excitation optical module of the smartphone-integrated analyzer passes through the reaction well of

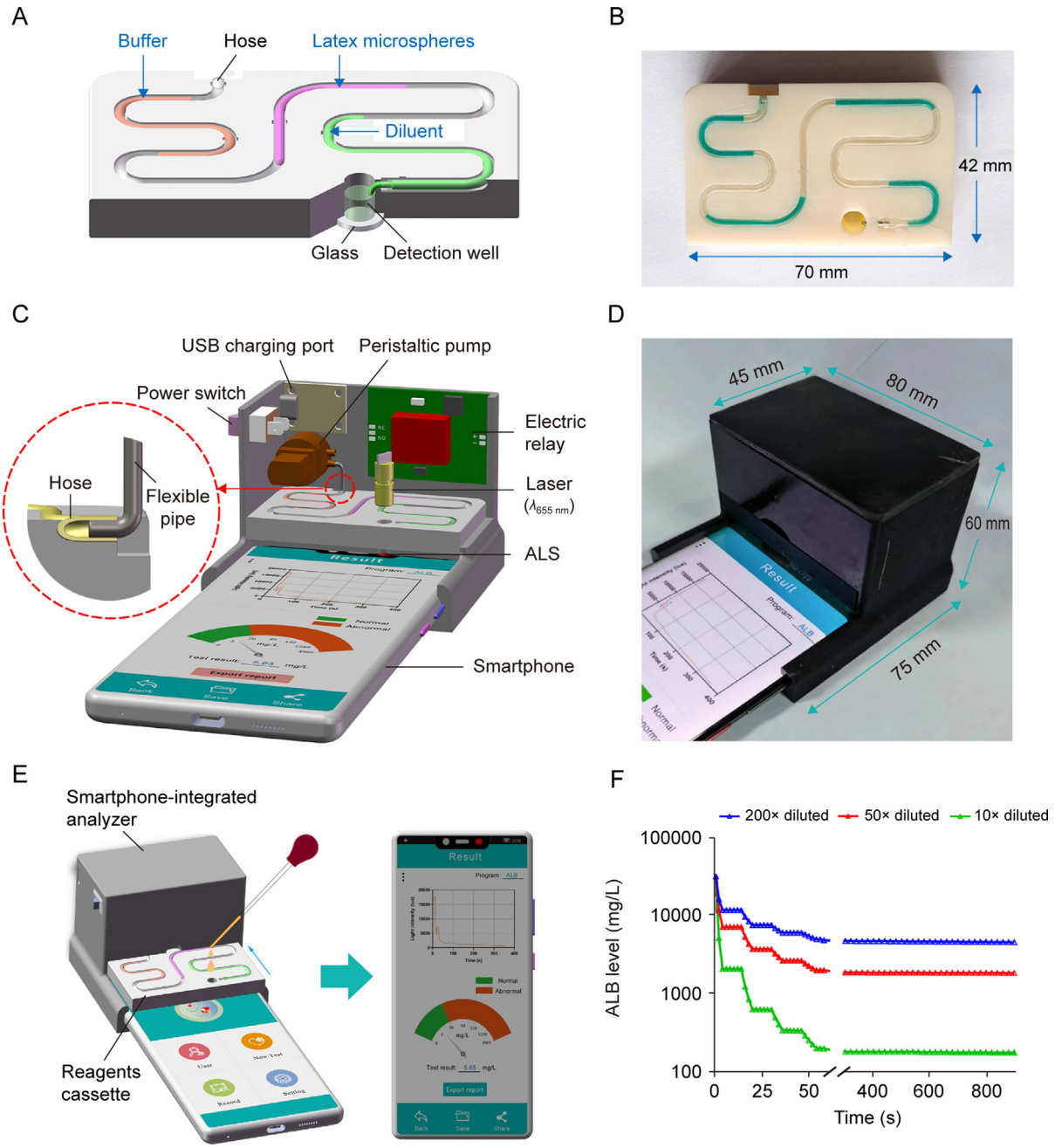

Fig. 2. Manufacture and performance verification of smartphone-integrated handheld automated biochemistry analyzer (sHABA). (A) Structure of the reagent cassette. (B) Practicality picture of the reagent cassette. (C) Partial section of smartphone-integrated analyzer. (D) Practicality picture of the smartphone-integrated analyzer. (E) Workflow for sHABA detection of albumin (ALB). (F) Feasibility and signal stability verification of sHABA. Fill the hoses within the reagent cassette with 10×, 50× and 200× diluted pigment, and run according to the set program (each cycle runs for 6 s and stops for 6 s, 4 cycles).

the reagent cassette and is received by the ambient light sensor (ALS) of the smartphone (Fig. 2E). The complete procedure is shown in Video 1. The latex microspheres used in the system have a broad absorption spectrum (Fig. S5). Here, we used a low-power laser with a wavelength of 655 nm as the light source. This specific wavelength was selected due to the potential presence of hemoglobin and bilirubin in urine, which strongly absorb visible light below 600 nm and could thus interfere with the accuracy of the results. Furthermore, the 655 nm laser is a readily available and economically viable light source, making it an optimal choice for POCT devices.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.jpha.2024.101041.

To assess the feasibility and reliability of the sHABA, we initially utilized a water-soluble blue pigment with a light absorption peak at 655 nm as a stand-in for the actual detection reagent in our experiments. We conducted tests on three distinct pigment gradients, which were created by diluting the pigment solution with water in ratios of 10-fold, 50-fold, and 200-fold. The pigment was divided into four parts and pre-loaded into the hose of the reagent cassette, and each part was separated by air. Then, insert the cassette into the analyzer, turn on the switch and start running. The sHABA running program was set as follows: run each cycle for 6 s, stop for 6 s, for 4 cycles. After continuously reading the signal for 15 min, the changes in the transmitted light intensity signal read by the smartphone ALS

can verify the feasibility of our proposed programming-driven reagents automatic addition and automatic signal reading. The results indicate that the transmitted light signal rapidly decreases during the operation of the peristaltic pump and remains unchanged during pauses. After the cyclic sample addition is completed, all reagents are injected into the reaction well, and the transmitted light signal intensity remains stable thereafter (Fig. 2F). These results demonstrate that sHABA can achieve automatic reagent addition and incubation, and has good signal reading stability.

In addition, to demonstrate the applicability of sHABA, different brands of smartphones were tested. We conducted tests on varying concentrations of albumin using different brand smartphones (Huawei Mate 20 Pro, Apple iPhone XR, Xiaomi 10, Samsung S10, and Vivo X30), recording the I value (intensity of light transmitted through the reaction solution) and the I_0 value (the optical intensity passing through an empty reaction well), and then calculated the ratio of I_0 to I. Despite variations in the absolute values of I and I0, the ratio I_0/I remained constant across different smartphone brands (Fig. S6). The use of Lambert's law (OD = Log I_0/I) to calculate absorbance is a standard practice in spectrophotometry. The fact that the absorbance values were the same across different devices suggests that sHABA can provide standardized results, which is essential for reliable diagnostic testing. The ability of sHABA to work with different smartphone brands implies that it can be adapted to a wide range of devices that are commonly available to consumers. This broad compatibility is a significant advantage, as it means that users do not need to invest in specialized hardware to utilize the sHABA system.

3.2. Validation of the sHABA using the ALB standard

To evaluate the performance of sHABA for ALB standard detection, initial experiments were conducted with spiked ALB standard in buffer solution at various concentrations: 0, 3.5, 7.0, 14.1, 28.1, 56.3, 112.5, 168.8, 225, 337.5, 450, 675, 900, and 1,200 mg/L. The color of the reaction well gradually darkens as the ALB level increases (Fig. 3A). Three different tests were conducted for each concentration of ALB, and a dose-response curve was plotted (Fig. S7), showing a clear linear relationship between the ALB concentration in the buffer and the corresponding transmission optical density value (i.e., OD value) measured by sHABA between 7 and 450 mg/L, with R^2 = 0.9908, the limit of detection (LOD) of 5.9 mg/L, and the limit of quantification (LOQ) of 6.4 mg/L (Fig. 3B). The linear relationship indicates that sHABA can accurately quantify ALB levels within a certain range, which is crucial for diagnostic purposes. The repeatability of sHABA in detecting ALB was also assessed, with three different concentrations of ALB (40, 100, 200 mg/L) tested using sHABA with 15 repetitions. Coefficients of variation (CV) values over 15 repetitions ranged from 6.24% to 7.27% (Fig. 3C), indicating excellent repeatability. High repeatability suggests reliability in the test results, which is essential for clinical decision-making.

3.3. Smartphone application (App) for ALB POCT

For ease of use, a smartphone app named *sHABA* was developed for data processing and analysis (Fig. 4). The app was installed and tested on a Huawei Mate20pro smartphone running Android 10.0.1. The user clicks the *sHABA* icon to start to run our App. A new window provides four options: User, New Test, Record and Setting (Fig. 4A). By clicking the “User” button on the homepage, users can access the user information interface, where they can add or edit their personal information and select their user profile (Fig. 4B). Clicking the “New Test” button on the homepage will initiate a new test and display the test results. This interface displays the detection concentrations of ALB (Fig. 4C). Users can obtain a detailed inspection report by clicking the “Export report” button at the bottom of this interface. By clicking the “Record” button on the homepage, users can access the results recording interface where they can view their historical detection results and monitoring curves for continuous detection (Fig. 4D). The program for controlling peristaltic pump and analyzing the data of detection results can be inputted and modified in the interface by clicking the “Setting button” (Fig. 4E). The app enhances the usability of sHABA, making it more accessible for non-expert users. Features like historical data tracking could be particularly useful for monitoring disease progression or treatment efficacy.

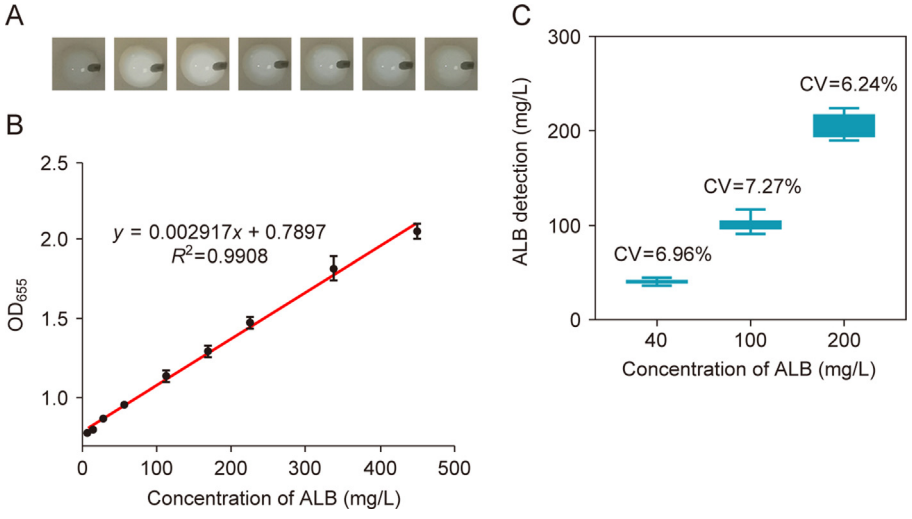

Fig. 3. Performance of smartphone-integrated handheld automated biochemistry analyzer (sHABA) for the detection of albumin (ALB) standard. (A) Images of reaction well for different ALB concentrations. (B) Calibration curve of sHABA for ALB detection; (C) repeatability evaluation of sHABA detection for ALB. Repeated testing was performed on three concentrations of ALB standards (40, 100, 200 mg/L), with coefficients of variation (CV) values of 6.96%, 7.27% and 6.24%, respectively.

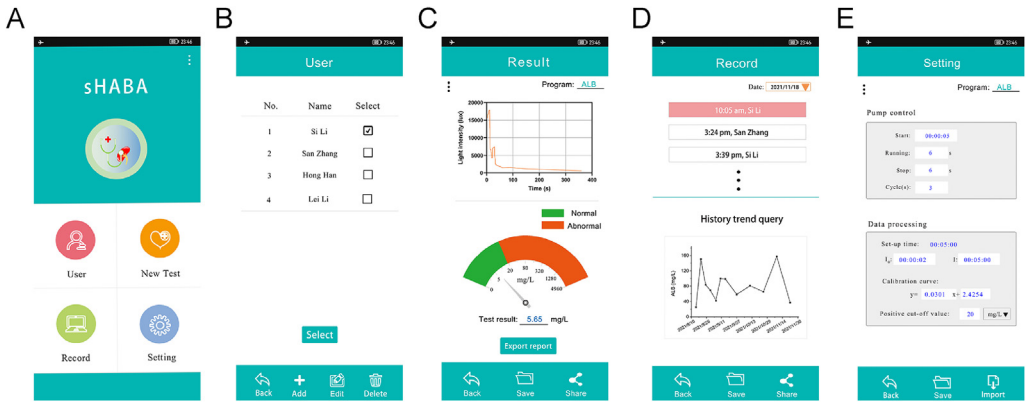

Fig. 4. The designed Android-based smartphone application (App) for albumin (ALB) point-of-care testing (POCT). (A) Main menu. (B) User information selection and addition. (C) A new test and the test results. (D) Record interface. (E) Setting interface.

3.4. *Performance of sHABA in the detection of ALB in urine samples*

Given its excellent performance in detecting ALB from PBS buffer, we further investigated the feasibility of applying sHABA in a real urine environment. 2 μL of urine sample was taken with a capillary tube and added to the reaction well, and then the reagent cassette was inserted into the analyzer. Under the control of the program, the diluent, latex microspheres and buffer inside the reagent cassette were added to the reaction well sequentially, and the smartphone app automatically read and analyzed the data for final results. 931 urine samples were tested. Results by sHABA showed good agreement with the clinical used automatic biochemical

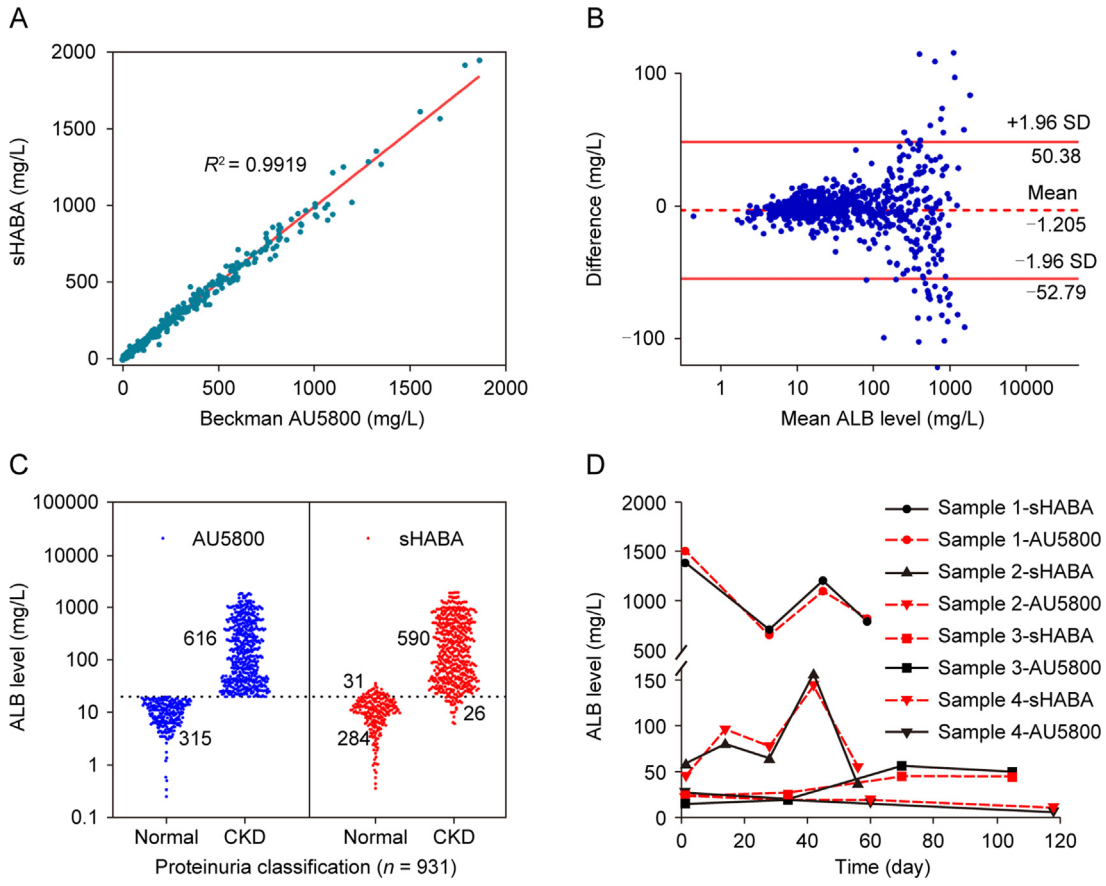

Fig. 5. Performance of smartphone-integrated handheld automated biochemistry analyzer (sHABA) in the detection of albumin (ALB) in urine samples. (A) Correlation of ALB detection by automatic biochemical analyzer (AU5800) and sHABA in urine samples (n = 931). (B) Bland–Altman analysis of ALB detection. Solid red lines represent 95% limits of agreement (−52.79–50.38 mg/L), and dotted lines represent bias (−1.205 mg/L). (C) Evaluation of renal injury degree by biochemical analyzer (AU5800) and sHABA in urine samples (n = 931). (D) Comparison of serial ALB level monitoring usingAU5800 and sHABA. CKD: chronic kidney disease; SD: standard deviation.

analyzer (AU5800) ($R^2 = 0.9919$) (Fig. 5A). The strong correlation with AU5800 validates sHABA as a reliable diagnostic tool for CKD. Bland–Altman analysis comparing the results of sHABA and AU5800 revealed a bias of −1.205 mg/L, with limits of agreement (LOA) ranging from −52.79 mg/L to 50.38 mg/L. Approximately 95.7% of the sample results fell within these LOA (Fig. 5B). Using an average ALB cut-off levels for proteinuria of 20 mg/L [10], the sensitivity and specificity of sHABA for diagnosing CKD are 95.78% (590/616) and 90.16% (284/315), respectively (Fig. 5C, and Table 1), indicating that sHABA is an accurate tool for early and accurate diagnosis of CKD. The differentiation between positive and negative samples here is based on the results from biochemical analyzers used clinically, adhering to the recommended cut-off value of 20 mg/L. However, there are slight variations when testing samples near the threshold, which can lead to discrepancies in the determination of positive or negative samples.

The effects of bilirubin on ALB testing were assessed by measuring ALB levels in urine samples with bilirubin concentrations ranging from 5 to 40 μM. The results from sHABA were consistently in line with those obtained by the AU5800, demonstrating excellent robustness of sHABA (Table S2). The ability to provide accurate results even in the presence of potential interferences increases the system's clinical utility. As a potential home diagnostic test product, the ability to monitor ALB levels over time could be invaluable for managing CKD and adjusting treatment strategies. The capacity for serial monitoring using POCT $_{testing}$was evaluated by testing the ALB levels of 4 patients with CKD major undergoing long-term treatment in Nanfang hospital. Trends in the ALB levels of these 4 patients, which were serially monitored for 59, 56, 105 and 118 days (Fig. 5D), were in agreement with those determined by the automatic biochemical analyzer (AU5800), indicating that sHABA was able to accurately track changes in ALB levels, reflecting the disease's dynamics. The long-term accuracy of sHABA suggests its potential as a home diagnostic tool for CKD patients.

Table 1
Performance of smartphone-integrated handheld automated biochemistry analyzer (sHABA) testing clinical samples.

Metric	Patient group ($n = 315$)[a]	Control group ($n = 616$)[a]
Test negative	284	26
Test positive	31	590
Sensitivity (%)	95.7 (590/616)	
Specificity (%)	90.16 (284/315)	
Accruacy (%)	93.88 (874/931)	

[a] The samples were categorized using the recommended cut-offs for urinary albumin levels (Normal: <20 mg/L; Albuminuria: >20 mg/L) based on clinical test results by Beckman AU5800.

3.5. Comparison of the sHABA with the other smartphone-based assays and other laboratory methods

Table 2 shows the comparison of sHABA with some currently published smartphone-based assays and laboratory methods for ALB detection. Compared with the smartphone-based colorimetric and fluorescence assay [27,28], the sHABA is similar in LOD and detection speed, but easier to operate. Compared with the smartphone-based dry chemistry method [29], the sHABA has comparable operational difficulty and detection speed but lower cost. Compared with electrochemical based method [30], sHABA does not have the LOD advantage, but is cheaper and less time-consuming. Compared with the immunologically based and HPLC-based laboratory methods, sHABA has higher LOD but much lower cost [31,32]. In addition, our method was validated with a large number of clinical samples, demonstrating its advantages in sensitivity and specificity.

4. Conclusion

In conclusion, we have successfully developed a cost-effective and automated smartphone integrated analyzer known as sHABA, designed for monitoring urinary albumin levels. The sHABA system has demonstrated its capability to conduct automatic albumin analysis, encompassing reagent addition, incubation, and result interpretation. When evaluating the system's performance for albumin detection, it showed consistency with clinical diagnostic instruments, indicating its potential as a reliable tool for medical practice. Innovations in sHABA compared to other POCT methods include automated reagent addition and incubation and the use of disposable cassettes, which contribute to its user-friendly design and cost-effectiveness. Moreover, by leveraging the connectivity features of smartphones, sHABA facilitates the delivery of professional medical guidance remotely, which could minimize the need for in-person clinic visits. It is important to note that while sHABA is currently configured to detect and quantify urinary albumin, it possesses the adaptability to be repurposed for the automatic detection of various biomarkers associated with chronic liver disease and cardiovascular conditions. This can be achieved by altering the detection reagents within the reagent cassette and adjusting the light source wavelength on the smartphone-integrated analyzer. The portability, affordability, and user-friendly design of sHABA make it a favorable solution for disease home self-testing, especially in areas with limited healthcare resources. In summary, the innovations of the sHABA platform mark a significant advancement in the early detection, management, and potentially home monitoring of chronic diseases, providing a promising avenue for improving patient care and reducing the burden on the healthcare system.

Table 2
Comparison of the smartphone-integrated handheld automated biochemistry analyzer (sHABA) with the other smartphone-based assays and laboratory methods.

Methods	Assays	LOD for albumin	Detection speed	Cost	Sensitivity (%)	Specificity (%)	Automatic
sHABA (this study)	Immunoturbidimetry	5.9 mg/L	Fast (<5 min)	Low ($1.5)	95.78 (590/616)	90.16 (284/315)	Yes
Other smartphone based methods	Colorimetric method	~10 mg/L	Fast (<5 min)	Low	ND	ND	No
	Fluorescence method	5–10 mg/L	Fast (<5 min)		88	ND	No
	Dry chemistry	~30 mg/L	Fast (<5 min)		ND	ND	Yes
	Electrochemical method	1.5 mg/L	Slow (>60 min)[a]	Fair	ND	ND	No
Immunologically based laboratory methods	Immunonephelometry	2 mg/L	Fair (10 min)	High	ND	ND	Yes
	ELISA	10 μg/L	Slow (>60 min)		ND	ND	Yes
HPLC laboratory method		2 mg/L	Slow (10–60 min)		ND	ND	No

HPLC: high performance liquid chromatography; ELISA: enzyme linked immunosorbent assay; LOD: limit of detection. ND: not determined.
[a] Although the signal reading time is within 0.5 min, the detection time should account for the time of electrode cleaning and the time of antibody re-coating before each detection.

CRediT authorship contribution statement

Ze Wu: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Peng Zhang:** Resources, Methodology, Investigation, Data curation. **Wei Xiao:** Validation, Resources, Funding acquisition. **Qian Chen:** Resources. **Wangrun Lin:** Investigation. **Peipei Chen:** Investigation. **Kangwei Chen:** Resources. **Qiangqiang Fu:** Writing – original draft, Methodology, Funding acquisition. **Zhijian Wang:** Validation, Resources. **Lei Zheng:** Supervision, Funding acquisition.

Declaration of competing interest

The authors declare that there are no conflicts of interest.

Acknowledgments

This work funding by the China Postdoctoral Science Foundation (Grant No.: 2021M701628), the National Natural Science Foundation of China (Grant No.: 82202625), Science and Technology Projects in Guangzhou, China (Grant No.: 2060206), President Foundation of Nanfang Hospital, Southern Medical University, China (Grant Nos.:2021B012, and 2021C050), National Science Fund for Distinguished Young Scholars, China (Grant No.: 82025024) and Key project of the National Natural Science Foundation of China (Grant No.: 82230080).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpha.2024.101041.

References

[1] E.F. Carney, The impact of chronic kidney disease on global health, Nat. Rev. Nephrol. 16 (2020), 251.
[2] V. Jha, A.Y.M. Wang, H. Wang, The impact of CKD identification in large countries: The burden of illness, Nephrol. Dial. Transplant. 27 (2012) iii32–iii38.
[3] K.E. Rudd, S.C. Johnson, K.M. Agesa, et al., Global, regional, and national sepsis incidence and mortality, 1990-2017: Analysis for the global burden of disease study, Lancet 395 (2020) 200–211.
[4] T.K. Chen, D.H. Knicely, M.E. Grams, Chronic kidney disease diagnosis and management: A review, JAMA 322 (2019) 1294–1304.
[5] J. Lv, L. Zhang, Prevalence and disease burden of chronic kidney disease, In: Liu, B.C., Lan, H.Y. and Lv, L.L., Eds. Renal Fibrosis: Mechanisms and Therapies, Springer, Singapore, 2019, pp. 3–15.
[6] P. Yomthiangthae, O. Chailapakul, W. Siangproh, Rapid urinary albumin detection using a simple redox cycling process coupled with a paper-based device, J. Electroanal. Chem. 911 (2022), 116230.
[7] R. Bodington, X. Kassianides, S. Bhandari, Point-of-care testing technologies for the home in chronic kidney disease: A narrative review, Clin. Kidney J. 14 (2021) 2316–2331.
[8] Q. Gao, S. Li, Intelligent point of care testing for medicine diagnosis, Interdiscip. Med. 2 (2024), e20230031.
[9] Y. Wang, S. Ma, Y. Chen, et al., Chronic kidney disease: Biomarker diagnosis to therapeutic targets, Clin. Chim. Acta 499 (2019) 54–63.
[10] H. Maeda, K. Sogawa, K. Sakaguchi, et al., Urinary albumin and transferrin as early diagnostic markers of chronic kidney disease, J. Vet. Med. Sci. 77 (2015) 937–943.
[11] B.K.I. Meijers, B. Bammens, K. Verbeke, et al., A review of albumin binding in CKD, Am. J. Kidney Dis. 51 (2008) 839–850.
[12] D.G. Warnock, Inclusion of albumin as a target in therapy guidelines: Guidelines for chronic kidney disease, Kidney Int. 66 (2004) S121–S123.
[13] H.J. Lambers Heerspink, R.T. Gansevoort, Albuminuria is an appropriate therapeutic target in patients with CKD: The pro view, Clin. J. Am. Soc. Nephrol. 10 (2015) 1079–1088.
[14] N. Cheeveewattanagul, C.F. Guajardo Yévenes, S. Bamrungsap, et al., Aptamer-functionalised magnetic particles for highly selective detection of urinary albumin in clinical samples of diabetic nephropathy and other kidney tract disease, Anal. Chim. Acta 1154 (2021), 338302.
[15] J.R. Mejia, J.E. Fernandez-Chinguel, G. Dolores-Maldonado, et al., Diagnostic accuracy of urine dipstick testing for albumin-to-creatinine ratio and albuminuria: A systematic review and meta-analysis, Heliyon 7 (2021), e08253.
[16] J.L. Camargo, G.M. Lara, A.E. Wendland, et al., Agreement of different immunoassays for urinary albumin measurement, Clin. Chem. 54 (2008) 925–927.
[17] O. Torffvit, J. Wieslander, A simplified enzyme-linked immunosorbent assay for urinary albumin, Scand. J. Clin. Lab. Investig. 46 (1986) 545–548.
[18] D.E. Busby, G.L. Bakris, Comparison of commonly used assays for the detection of microalbuminuria, J. Clin. Hypertens. 6 (2004) 8–12.
[19] Z. Li, Y. Zhao, X. Lv, et al., Integrated brain on a chip and automated organ-on-chips systems, Interdiscip, Med. 1 (2023), e20220002.
[20] L. Paloheimo, M. Pajari-Backas, E. Pitkänen, et al., Evaluation of an immunoturbidimetric microalbuminuria assay, J. Clin. Chem. Clin. Biochem. 25 (1987) 889–892.
[21] A.S. Bargnoux, A. Barrot, P. Fesler, et al., Evaluation of five immunoturbidimetric assays for urinary albumin quantification and their impact on albuminuria categorization, Clin. Biochem. 47 (2014) 250–253.
[22] N. Rifai, K. Gubar, L.M. Silverman, Immunoturbidimetry: An attractive technique for the determination of urinary albumin and transferrin, Clin. Biochem. 20 (1987) 179–181.
[23] J. Qian, J. Zhang, Z. Wu, et al., Special issue: Smart flow control in micro scale, Processes 8 (2020), 550.
[24] C. Wang, Z. Wu, B. Liu, et al., Track-etched membrane microplate and smartphone immunosensing for SARS-CoV-2 neutralizing antibody, Biosens. Bioelectron. 192 (2021), 113550.
[25] Y.C. Chang, X. Ge, L. Wang, et al., An ultra low-cost smartphone device for in situ monitoring of acute organophosphorus poisoning for agricultural workers, Sens. Actuat. B Chem. 275 (2018) 300–305.
[26] J. Tan, S. Wu, Q. Cai, et al., Reversible regulation of enzyme-like activity of molybdenum disulfide quantum dots for colorimetric pharmaceutical analysis, J. Pharm. Anal. 12 (2022) 113–121.
[27] A.F. Coskun, R. Nagi, K. Sadeghi, et al., Albumin testing in urine using a smartphone, Lab Chip 13 (2013) 4231–4238.
[28] A. Mathaweesansurn, N. Maneerat, N. Choengchan, A mobile phone-based analyzer for quantitative determination of urinary albumin using self-calibration approach, Sens. Actuat. B Chem. 242 (2017) 476–483.
[29] R. Thakur, P. Maheshwari, S. Kumar Datta, et al., Smartphone-based, automated detection of urine albumin using deep learning approach, Measurement 194 (2022), 110948.
[30] Z. Shi, C. Dai, P. Deng, et al., Smartphone-based portable photoelectrochemical biosensing system for point-of-care detection of urine creatinine and albumin, Lab Chip 23 (2023) 3424–3432.
[31] W.D. Comper, G. Jerums, T.M. Osicka, Differences in urinary albumin detected by four immunoassays and high-performance liquid chromatography, Clin. Biochem. 37 (2004) 105–111.
[32] C. Aybay, R. Karakuş, Measurement of urine albumin levels with a monoclonal antibody based in-house ELISA, Turk. J. Med. Sci. 33 (2003) 1–5.