Development of Non-invasive Biochemical Device for Monitoring the Lithium Level from Saliva for Bipolar Disorder Patients

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Summary

In this paper, we present a novel biochemical sensing device which is monitoring lithium level from saliva for a non-invasive measurement. According to the American Psychiatric Association (APA) 2002 guidelines for treating bipolar disorder, the first-line therapy for bipolar patients with severe mania or mixed episodes is an antipsychotic medication combined with either lithium or the anticonvulsant Depakote[1]. Lithium (brand names Eskalith, Lithobid, Lithonate, and Lithotabs) is the most widely used and studied medication for treating bipolar disorder for reducing the severity and frequency of mania depression[2]. But it is also a very difficult and potentially dangerous drug for patients. Lithium's therapeutic dose is uncomfortably close to its toxic dose, meaning it is rather easy to take too much lithium by mistake and become poisoned. Therefore, patients need to have regular tests with blood serum to monitor the levels of lithium based medication.
This paper presents part of our work in developing a low cost, non-invasive portable healthcare technology to put more control into the hands of patients so that the earliest signs of problems can be detected and corrected by monitoring the drug level from the saliva.

Motivation

A very sensitive analytical method was investigated for the spectrofluorimetric determination of lithium base on its reaction with 1,4-dihydroxyanthraquinone (Quinizarin)[3]. The fluorescence is measured at 620 nm with an excitation wavelength of 590 nm. A portable biochemical device was developed to measure the intensity of fluorescence. The light source (λ_{center} = 590nm, 50mW) and photo detector (OPT101: Texas Instruments) were configured at 90 degree angle in the opaque cuvette holder as shown in Fig. 1.

Results

Prototype of portable device has been developed including photo detector for spectrofluorimetric sensing as shown in Figure 2. The receiver unit is connected with USB port of laptop/PC. Saliva sample was tested using portable device in order to validate the feasibility of saliva as a sample to detect lithium ions. According to the clinical tests, the salivary lithium concentration is 2.2 ~ 2.5 times higher than serum lithium with significant correlation factor. Unstimulated saliva was collected and known concentration of Li^+ was spiked into the saliva to prepare the Li^+ doped saliva. Using lithium doped salivary sample, calibration was performed. Results presented in Fig. 3 show calibrations obtained from different saliva samples collected on different days. Similar results were obtained with linear range of detection between 0.25mM ~ 6.0 mM of Li^+ and R^2=0.990. When we consider the therapeutic range of lithium in serum is 0.6 ~ 1.0 mM, the expected salivary lithium concentration would be higher than lithium in serum. Linear range of the proposed method covers sufficiently the therapeutic range of lithium drugs.

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[2] M. E. Thase, and G. S. Sachs, "Bipolar Depression: Pharmacotherapy and Related Therapeutic Strategies," Biological Psychiatry, Vol. 48(6), pp. 558-572, 2000.

[3] M. R. Ceba, A. F. Gutierrez and C. M. Sanchez, "Some observations on the use of 1,4-dihydroxyanthraquinone as a fluorometric reagent for traces of lithium," Microchemical Journal, Vol. 32(3), pp. 286-292, 1985.

Figures

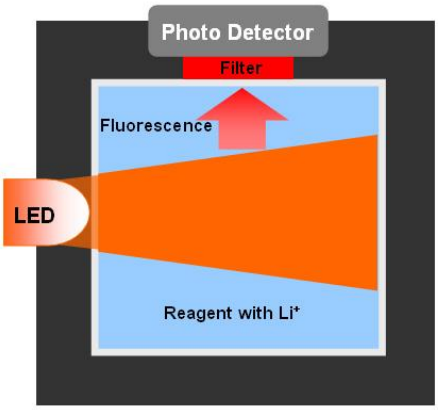

Fig. 1: Schematic of the optical sensing module for the measurement of fluorescence.

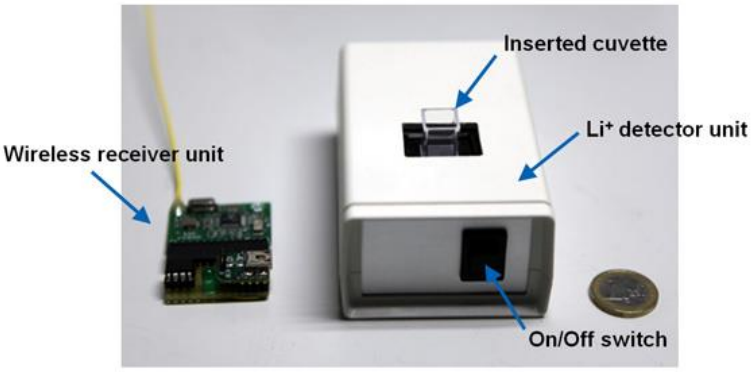

Fig. 2: Developed portable biochemical device for measuring the concentration of lithium in salivary sample.

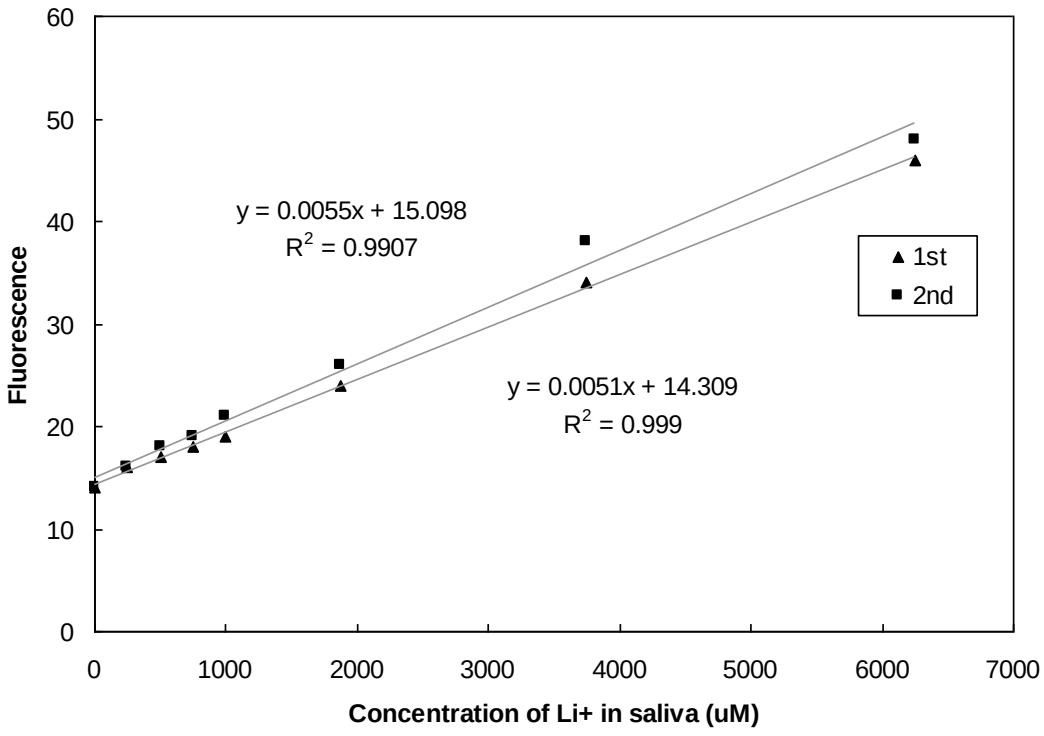

Fig. 3: Calibration results from Li+ doped saliva with portable device.