Simple device for urinary uric acid measurements in gout patients

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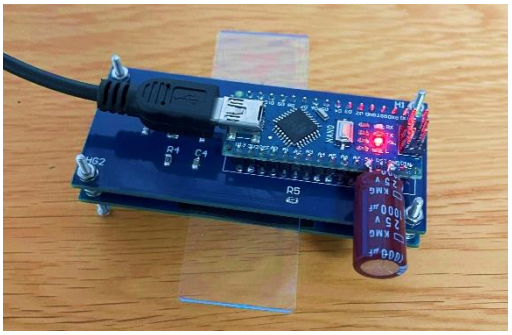

Figure 1- First prototype.

[Problem Description]

Gout is a type of inflammatory arthritis with an estimated prevalence of 41 million in 2017,[(1)] including my own younger brother. It is characterized by high levels of serum uric acid (hyperuricemia). Uric acid is a product of the purine metabolism: high consumption of purines is the most common cause. Other causes include dysfunction in the excretory system through renal and GI pathways. Monitoring uric acid levels in the blood and urine enables precise medication interventions and is crucial to prevent painful gout attacks.

The current methods for monitoring serum and urinary uric acid are invasive, costly, and time-consuming. This initial project focuses on simplifying urinary uric acid measurements, with the application of the same principles for serum measurements in mind.

Today, measurement of urinary uric acid is done by biochemical analysis. Uricase and peroxidase is added to produce a dye, and a spectrophotometer is used to measure absorbance at 520 nm[(2)].

Global gout prevalence is expected to grow to 96 million in 2050[(3)], especially in rapidly developing countries with an exploding middle class. This situation calls for a cheap, simple, and widely accessible solution for closely monitoring uric acid levels.

In this executive summary, a prototype device which uses UV light to enable chemical-free measurement of urinary uric acid is discussed.

[Solution Concept]

The measurement of 24-hour urinary uric acid excretion is frequently used to evaluate disease status. However, 24-hour urine collection is inconvenient and frequently unreliable. Choi, et al[(4)] showed that the uric acid – creatinine ratio in spot urine has a significant correlation with 24-hour urinary excretion. According to Lin, et al[(2)], uric acid has a high absorbance spectrum at 290-300 nm, with very low interference from other substances commonly found in human urine.(figure 2) The definition of the absorbance of light in a medium, in conjunction with Beer-Lambert's law allows for the estimation of uric acid content through calibration of the device.

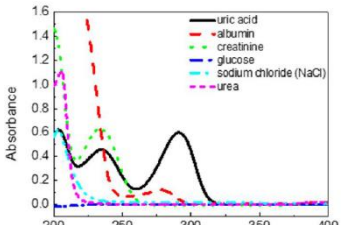

Figure 2 - absorbance spectra of common urine content.

$$A = -\log\left(\frac{I}{I_0}\right) = \varepsilon c l \;\therefore c = \frac{-\log\left(\frac{I}{I_0}\right)}{\varepsilon l}$$

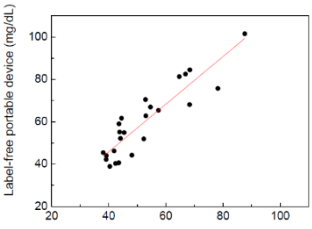

Figure 3 - accuracy of protype in (2)

(A: absorbance, I: transmitted light intensity, I_0: incident light intensity, ε: molar attenuation coefficient – to be calculated in calibration, c: concentration, l: optical path)

Lin, et al.[(2)] outlined and tested a prototype which measures the absorbance of gout patients' urine at that wavelength to estimate the concentration of uric acid in each sample, with a high coefficient of determination (0.8083) (figure 3). No details on the design of the prototype device were given in the paper, and there was no response upon contacting the authors. Therefore, I designed and constructed a device that will estimate the urinary uric acid with the same principles described in the paper, completely from scratch. This device has the potential to allow patients to monitor their uric acid any time of the day, chemical-free, and send data to their clinicians to allow for more informed interventions.

[Reduction to practice]

The device consists of two PCBs with a gap in between for urine samples on microscope slides to be inserted.

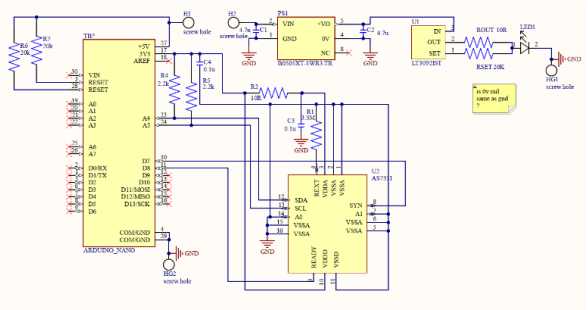

Figure 4- Circuit schematic for first prototype.

UV light is emitted from the bottom board, shines through the sample and measured by the sensor on the top board. The analogue data of UV light strength is converted to a digital value, and absorbance is calculated and displayed on the Arduino Serial Monitor. The device was designed on Altium Designer, the PCBs were manufactured by PCB Way, and components were sourced from Digi-Key. The software was developed with some sourcecode from SparkFun Electronics under MIT license. The total cost for one whole device was appox. 45 USD. This device may not completely replace spectrophotometers used in hospitals, but with more improvements it could be used at homes to provide important insight to help clinicians.

The functionality of the device was verified by comparing the absorbance of a healthy subject's urine and a gout patient's urine. This patient was known to underexcrete uric acid due to a possible defect in the GI excretory pathway. Comparison of values showed that the absorbance value was higher in the healthy subject, which is consistent with the higher concentration of uric acid in their urine. Further validation is required.

[Pathway to implementation]

Calibration of device – using pure uric acid samples, I aim to calibrate the device using the principles presented in the equation, to enable estimation of uric acid values with the device. As this is a personal holiday project with no funding, high costs and long delivery times of pure samples prevented the completion of this step before initial submission: I am on course to have this done by the time of the final round.

Addition of creatinine measurement – since the uric acid to creatinine ratio is commonly used for excretion estimation, the function of measuring creatinine based on its absorption spectrum is necessary. Research suggests this is around 520nm.

Increased accuracy and better user interface – improving the circuit design and creating a better UI is essential.

[References]

Works Cited

(1) Mattiuzzi, Camilla, and Giuseppe Lippi. “Recent Updates on Worldwide Gout Epidemiology.” *Clinical Rheumatology*, vol. 39, no. 4, 13 Dec. 2019, pp. 1061–1063, https://doi.org/10.1007/s10067-019-04868-9. Accessed 10 Feb. 2024.

(2) Lin, Tsung-Jui, et al. “Label-Free Uric Acid Estimation of Spot Urine Using Portable Device Based on UV Spectrophotometry.” *Sensors*, vol. 22, no. 8, 14 Apr. 2022, p. 3009, https://doi.org/10.3390/s22083009. Accessed 10 Feb. 2024.

(3) Cross, Marita, et al. “Global, Regional, and National Burden of Gout, 1990–2020, and Projections to 2050: A Systematic Analysis of the Global Burden of Disease Study 2021.” *Social Science Research Network*, 16 June 2023, ssrn.com/abstract=4478194. Accessed 10 Feb. 2024.

(4) Choi, S, et al. “FRI0248 Validity of Random Urinary Uric Acid-To-Creatinine Ratio for Estimating 24-Hour Urine Uric Acid Excretion in Patients with Gout.” *Annals of the Rheumatic Diseases (ARD)*, 1 June 2018, https://doi.org/10.1136/annrheumdis-2018-eular.5005. Accessed 10 Feb. 2024.