Ocular Glucose Biosensing Using Boronic Acid Fluorophores

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Abstract

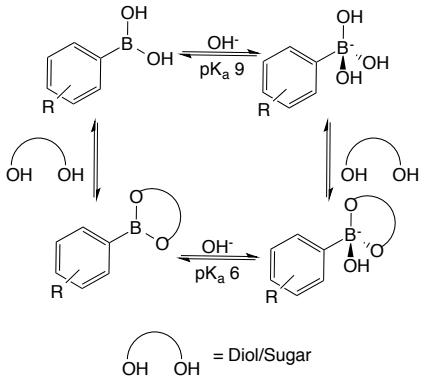
Boronic acids (BAs) are well-known for their interactions with diol-containing compounds like glucose. Fluorescent moieties are commonly incorporated into a BA derivative's framework to monitor the effect of varying glucose concentrations in a given environment. Hence, a novel carboxylic acid fluorescent BA derivative, o-COOHBA, has been investigated for glucose sensing, in solution and when immobilised onto a polydimethylsiloxane (PDMS) "lens"-like surface. This approach aims to develop smart-contact lenses that will allow people suffering from diabetes to track their condition continuously and non-invasively in real-time.

1. Introduction

Diabetes is a worldwide incurable disease known to have acute and chronic health effects[1-2]. This disease affects the cardiovascular and peripheral nervous systems, kidneys, and can also be fatal in some cases[1-2]. Blindness, heart or kidney failures are among the most common life-threatening effects of diabetes[2]. Monitoring physiological blood-glucose concentrations is a means of managing the disease, however few non-invasive continuous monitoring methods currently exist[1-2]. Consequently, there is considerable interested in using aqueous ocular fluid as a sample medium for tracking the disease marker glucose.

2. Sensing Mechanism

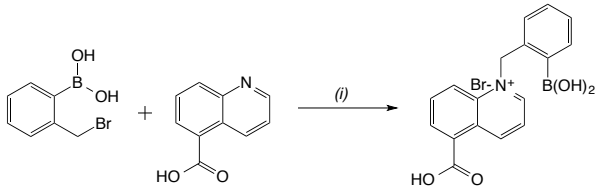
The Lewis acidic BA moiety of the sensor is known for its strong interaction with electron-rich diols, like sugars[1-2]. On interaction with sugars, *e.g.* glucose, the fluorescent BA form is transformed into the anionic boronate form, which is non-fluorescent, leading to a decrease in the fluorescence intensity with increasing sugar concentrations[1-2].



Scheme 1: Sensing mechanism for BA derivatives.

3. Synthesis of *o*-COOHBA Sensor

A novel BA sensor, *o*-COOHBA, was synthesized *via* a one-step nucleophilic substitution reaction that required equimolar quantities of BA and quinoline derivatives, as seen in Scheme 2. The successful formation of *o*-COOHBA was confirmed by ^{1}H NMR.



Scheme 2: Synthesis of o-COOHBA; (*i*) anhydrous dimethylsulfoxide, N_2, 70 ^{0}C for 48h.

4. Fluorescence of *o*-COOHBA

Fluorescence measurements were performed on a Jasco FP-8300 Spectrophotometer using a precision cell made from quartz with 10 mm path length. The excitation wavelength required was 380 nm with a corresponding emission wavelength of 485 nm.

On increased glucose concentrations, a decrease in fluorescence intensity was observed in the range of 0-10 mM in solution and similarly, in the range of 0-5 mM when anchored to a PDMS surface, corresponding to the ocular-glucose concentrations for diabetics, ~50 µM – 5 mM[2]. All tests were carried out at an ambient temperature using a pH 7.4 phosphate buffer.

5. Conclusion

In both solution studies and when anchored on to the PDMS surface, a decrease in fluorescence intensity was observed on increased glucose concentrations. The excitation wavelength of 380 nm is also advantageous, as it lies close to the visible-region of the electromagnetic spectrum, which allows for the use of cheap, readily available LEDs as excitation sources. The carboxylic acid substituent was desirable for immobilizing the BA sensor onto a wide variety of polymeric substrates.

6. References

[1] H. Fang, G. Kaur, B. Wang, *Journal of Fluorescence*, *14(5)*; 481-489, 2004
[2] R. Badugu, J. R. Lakowicz, C. D. Geddes, *Journal of Fluorescence*, *14(5)*; 617-633, 2004