Journal of Diabetes Science and Technology
Volume 5, Issue 1, January 2011

ORIGINAL ARTICLES

The Design and Development of Fluorescent Nano-Optodes for *in Vivo* Glucose Monitoring

Mary K. Balaconis, B.S.,[1] Kelvin Billingsley, Ph.D.,[2] J. Matthew Dubach, B.S.,[1]
Kevin J. Cash, Ph.D.,[3]and Heather A. Clark, Ph.D.[3]

Abstract

Background:

The advent of fluorescent nanosensors has enabled intracellular monitoring of several physiological analytes, which was previously not possible with molecular dyes or other invasive techniques. We have extended the capability of these sensors to include the detection of small molecules with the development of glucose-sensitive nano-optodes. Herein, we discuss the design and development of glucose-sensitive nano-optodes, which have been proven functional both *in vitro* and *in vivo*.

Methods:

Throughout the design process, each of the sensor formulations was evaluated based on their response to changes in glucose levels. The percent change in signal, sensor reversibility, and the overall fluorescence intensity were the specific parameters used to assess each formulation.

Results:

A hydrophobic boronic acid was selected that yielded a fully reversible fluorescence response to glucose in accordance with the sensor mechanism. The change in fluorescence signal in response to glucose was approximately 11%. The use of different additives or chromophores did not improve the response; however, modifications to the plasticized polymeric membrane extended sensor lifetime.

Conclusions:

Sensors were developed that yielded a dynamic response to glucose and through further modification of the components, sensor lifetime was improved. By following specific design criteria for the macrosensors, the sensors were miniaturized into nano-optodes that track changes in glucose levels *in vivo*.

J Diabetes Sci Technol 2011;5(1):68-75

Author Affiliations: [1]Department of Bioengineering, Northeastern University, Boston, Massachusetts; [2]Department of Chemistry, Stanford University, Stanford, California; and [3]Department of Pharmaceutical Sciences, Northeastern University, Boston, Massachusetts

Abbreviations: (ARS) alizarin red S, (DCM) dichloromethane, (DMF) N,N-dimethylformamide, (DOS) bis(2-ethylhexyl) sebacate, (DPP) dipentyl phthalate, (EDC·HCl) N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride, (IPA) 2-propanol, (ISE) ion-selective electrode, (NPOE) 2-nitrophenyl octyl ether, (PBS) phosphate-buffered saline, (PCL) polycaprolactone, (PMMA(COOH)$_2$) α,ω-dicarboxy terminated poly(methyl methacrylate), (PUR) polyurethane, (PVC-COOH) poly(vinyl chloride) carboxylated, (PVC) poly(vinyl chloride), (P(VDC/AN) poly(vinylidene chloride/acrylonitrile), (PY) pyridine, (7,8-DHMC) 7,8-dihydroxy-4-methylcoumarin, ($SOCl_2$) thionyl chloride, (TBAB) tetrabutylammonium bromide, (TBAC) tetrabutylammonium chloride, (TBAI) tetrabutylammonium iodide, (TDMAC) tridodecylmethylammonium chloride, (TEP) tris(2-ethylhexyl) phosphate, (THF) tetrahydrofuran anhydrous

Keywords: boronic acid, bulk optodes, fluorescent sensors, glucose monitoring

Corresponding Author: Heather A. Clark, Ph.D., Department of Pharmaceutical Sciences, Northeastern University, Room 110 Mugar Life Sciences Building, 360 Huntington Avenue, Boston, MA 02115; email address h.clark@neu.edu