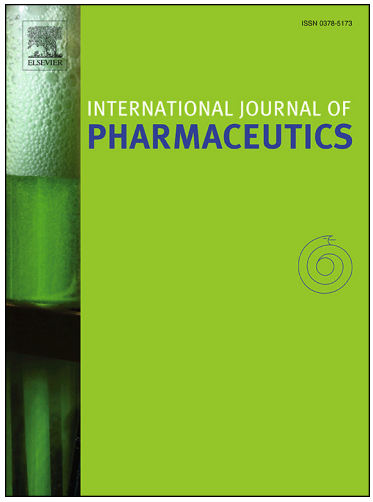

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A Review of Implantable Biosensors for Closed-Loop Glucose Control and Other Drug Delivery Applications

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Abstract

Closed-loop drug delivery promises autonomous control of pharmacotherapy through the continuous monitoring of biomarker levels. For decades, researchers have strived for portable closed-loop systems, capable of treating ambulatory patients with chronic conditions such as diabetes mellitus. After years of development, the first of these systems have left the laboratory and entered commercial use. This long-awaited advance reflects recent development of chronically stable implantable biosensors, able to accurately measure biomarker levels *in vivo*. This review discusses the role of implantable biosensors in closed-loop drug delivery applications, with the intent to provide a resource for engineers and researchers studying such systems. We provide an overview of common biosensor designs and review the principle challenges in implementing long indwelling sensors: namely device sensitivity, selectivity, and lifetime. This review examines novel advances in transducer design, biological interfaces, and material biocompatibility, with a focus on recent academic and commercial work which provide successful strategies to overcome perennial challenges. This review focuses primarily on the topics of closed-loop glucose control, and continuous glucose monitoring biosensors, which make up the overwhelming majority of published research in this area. We conclude with an overview of recent advances in closed-loop systems targeting applications outside blood glucose management.

Keywords: Closed-loop drug delivery, biosensor, implantable sensor, continuous glucose monitoring, enzymatic sensor