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Electronic drug delivery systems: An overview

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ABSTRACT

Patient compliance is an important consideration in designing drug delivery systems which is also driving the advances and innovations in drug delivery. A report by BCC Research, a US – based market research firm, estimates that the global market for advanced drug delivery technologies is poised to grow to approximately $227 billion by 2020. Amongst the various drug delivery technologies, electronic drug delivery systems (EDDS) represents an exciting trend in the development of drug delivery systems that are portable, interactive, wirelessly connected and allow patient-administered therapy reducing overall healthcare cost. Insulin pump is the most commonly used EDDS and captures the largest share of the global EDDS market. The improvement of patient adherence when using prescribed medication is one of the driving force in the development of EDDS. Furthermore, EDDS have shown the potential to provide targeted drug delivery to particular sites in the body. Although various drug delivery devices are available in the market, this review focuses on electronic drug delivery devices. The advantages and disadvantages associated with these devices as well as future perspectives of the EDDS are also discussed.

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1. Introduction

Innovative scientific and technological advances in electronic drug delivery systems (EDDS) are making a momentous breakthrough in pharmaceutical drug delivery within the healthcare setting [1]. EDDS have a small share of the global advanced drug delivery technologies market which is estimated to grow to approximately $227 billion by 2020, nevertheless it is one of the most exciting and fast growing market [2]. EDDS currently available in the market or in commercial development are presented in Table 1. This novel system of drug delivery and administration presents many advantages over traditional delivery systems including accurate and specific dose delivery, improved medication compliance and therapeutic outcomes, patient monitoring, and reduced side effects [3]. It is estimated that medication non-adherence is a $290-billion problem and the percentage of patients who fail to take their medication as prescribed is as high as 50% [4].

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Table 1
Electronic drug delivery systems in commercial development or on the market.

EDDS	Technology/Design	Company/ Institute	Status
Abilify/ Proteus™	Ingestible sensor, activated by stomach fluid, sends signal to an external patch, which tracks medication taking, steps, activity, sleep and heart rate, and is delivered to "discover app," which can be shared with a third party.	Proteus Digital Health	FDA rejected the NDA in 2016, filed as first drug/device tablet
SmartPill™	Ingestible capsule that measures pressure, pH and temperature as it travels through the GI tract to assess GI motility.	Given Imaging (now Covidien)	FDA approval, 2006
IntelliCap®	Capsule containing drug reservoir, pH, temperature sensors, microprocessor and transmitter. Releases drugs to the defined region of GI tract and provides two way real-time wireless communication	Medimetrics, Inc.	Preclinical trials
Microchip™	Implantable chip with multiple microreservoirs which hold drugs, activated by wireless signals.	Microchips Biotech	In clinical trials
MiniMed 670G System™	Consists of a continuous glucose monitor (CGM) that measures the user's glucose levels for up to seven days, an insulin pump that delivers insulin to the user and can automatically adjust the delivery of insulin using a mathematical equation, or algorithm that incorporates information from the CGM.	Medtronic MiniMed Inc.	FDA approval, 2016
SmartDose™	Single-use, electronic wearable injector that adheres to a patient's body. Pre-programmed to deliver high volumes of viscous or sensitive drug products. Primary container molded from Daikyo Crystal Zenith® cyclic olefin polymer, which eliminates potential problems with glass delamination.	West Pharmaceutical Services, Inc.	FDA approval, 2016
Imperium™ Platform	Prefilled, disposable, multi-day wearable insulin pump that does not require filling or assembly by the patient. Can include wireless connectivity systems, such as Bluetooth LE, to integrate with smartphone apps for patient reminders and status updates to tailor insulin therapy.	Unilife Corporation	Searching prospective partners for clinical trials
TriGrid™ Array	Electroporation based technology. Utilizes an array of penetrating electrodes configured in a pattern of interlocking triangles arranged to form a diamond shape around an integrated central injection needle to enhance electrical field uniformity at the site of application.	Ichor Medical Systems	Collaboration with Janssen Pharmaceuticals, Inc. for commercializing DNA-based vaccine
SonoPrep™	Applies low frequency ultrasound to a patient's skin for approximately 15 s to create imperceptible, reversible micro-channels through the stratum corneum. This is followed by application of drug formulation.	Sontra Medical	FDA approval, 2004
BETACONNECT®	Electronic auto-injector with automatic needle insertion and retraction, customizable injection speed and depth, built-in injection reminders. Can capture data from every injection and send it wirelessly to myBETAapp®	Bayer Healthcare	FDA approval, 2015 FDA approval for sBLA in 2017
InPen™	Reusable injector pen with an intuitive smartphone interface. Keeps track of insulin intake, calculate dosage and manage how much is in reserve.	Companion Medical Inc.	FDA approval, 2016
Enable Injections	Disposable body-worn bolus injector to deliver high-viscosity/volume payloads up to 20 cc to the subcutaneous tissue via pressing a button. A "pause" function allows the user to pause the injection if experiencing any pain. Automatically warms the drug and can be used immediately.	Enable Injections	In clinical trials
Amber Pushclick® Technology	Single-use, disposable auto injector, activated by pushing against the injection site. Audible, visual and tactile feedback, permanently hidden needle.	SHL Medical Products	Available for licensing to prospective clients
LISA™	Reusable auto-injector that provides user-selected injection speeds, needle free disposal and option of Bluetooth connectivity. Can be combined with proprietary EZMix platform for one step drug reconstitution and Bluetooth connectivity.	Unilife Corporation	Available for licensing to prospective clients

The automated delivery of EDDS can provide precise dose, route, frequency, and timing of medication which subsequently may improve adherence to complicated regimens and lessen anxiety associated with administration [5,6].

Healthcare providers continuously strive to reduce and prevent side effects caused by drugs, and EDDS are able to reduce systemic side effects by providing drug delivery targeted to particular sites in the body that are difficult to reach, such as the brain and specific regions of the gastrointestinal (GI) tract [1]. EDDS that are required to be implanted into the body are invasive in nature, require special expertise for the placement of the device and may cause scar formation at the site of implantation. Other disadvantages of EDDS include the danger of device failure, biocompatibility issues, potential adverse reactions and the high cost involved in the design and development. Since electronics is an integral part of the EDDS, educating the patients who are averse to the use of technology, in the proper use of the electronic device might present significant challenges. Additional safety and stability testing and pharmaceutical characterization may also be required because of the electronics involved drug delivery device. Available electronic drug delivery devices include, but are not limited to microchips, electronic capsules, transdermal patches, insulin pumps, and auto-injectors. Each of these devices is individually unique in its own system of drug delivery and has the potential to offer distinctive advantages over traditional delivery systems. A brief discussion of the above electronic drug delivery systems are presented in this article.

2. Microchip devices

A microchip is an implantable drug delivery device that stores and releases drug from small reservoirs [7–10]. The electronic device consists of hundreds of micro reservoirs each of which is capped with a metal membrane with the final circuitry controlled by a microprocessor or input source [11]. The control circuitry consists of a timer, demultiplexer, microprocessor an input source. A thin film micro battery can be used as a power source [12]. Small doses of therapeutic drugs or chemicals are stored into each of the micro reservoirs. These drugs should be potent and highly soluble in order to minimize the size of the implant [7]. Upon application of a tiny electric current through a wireless signal, the metal cap is removed releasing a single dose inside the body. Thus, microchips deliver a constant release of drug over a longer period of time by applying a small electric current between a specific reservoir and the metal covering it. The drug release is controlled through a pre-programmed dosing schedule. Furthermore, sensors can be built