Extended Abstract

Journal of Pharmacology Research

2018

Vol.1 No.2

Pharmacology 2018: Dissolving microneedles for the delivery of therapeutics - Laura E. Gonzalez Garcia - Future Industries Institute

Laura E. Gonzalez Garcia
Future Industries Institute, University of South Australia
School of Engineering, University of South Australia

Abstract

The application of nanotechnology in health sciences has experienced an exponential growth over the last 25 years with special focus on drug delivery systems. Transdermal delivery has recently gained importance for its numerous advantages, which include sustainable release, bypass of the pre-systemic hepatic metabolism and patient compliance. Microneedles are designed to circumvent the skin barrier to enhance transdermal drug delivery. They have been produced in various geometries (cone, cylinder, triangular prism, etc) and materials such as silica, polymers or metals. Microneedles made from sugars or water soluble polymers are dissolvable in the skin and release the drug cargo leaving no sharp waste behind. Moreover, polymer microneedles can incorporate larger drug load than other type of needles such as coated or hydrogel swelling microneedles. These dissolving microneedle arrays have been applied in various pharmacological sectors such as gene therapy, vaccine delivery or drug delivery.

However there is still a need of clinical and pre-clinical research before these devices can be released into the market. An essential challenge is to tailor the microneedles dissolution rate to control the release of therapeutics irrespective of the polymeric material. There is also a need to reduce the risk of skin infections during the insertion as microneedles create small pores on the skin.

Our research focuses on the development of plasma polymerized surface engineered microneedles for a controlled dissolution and controlled drug release. This one-step, environmentally friendly and substrate independent technique will also ease the industrial manufacture. Furthermore these surfaces can be functionalizing to confer antibacterial properties to our microneedles patches to hinder infections and skin damage.

Introduction

Compared to more traditional routes like oral administration and hypodermic injection, transcutaneous drug delivery through chemical permeation of the skin, iontophoresis, ultrasound, microneedle treatment, or various other strategies has the potential to provide many practical and clinical advantages.1 Relative to parenteral injection, transcutaneous delivery is non-invasive, potentially allowing for rapid, pain-free administration either by minimally trained health care providers, or through self-administration.2, 3 Transcutaneous delivery systems may reduce the generation of dangerous medical waste and inhibit the spread of disease known to occur through needle-reuse and needle-based injury.4, 5 Further, dry storage of systems designed for topical application can also provide enhanced drug stability, enabling transport of environmentally sensitive biological therapeutics without the necessity for refrigeration. This is a key issue as the requirement of “cold chain” distribution increases costs and inherently limits the availability of therapies throughout the developing world.2 Transcutaneous therapeutic administration also has the potential to enhance the clinical effectiveness of treatment, by allowing for more efficient delivery of drugs susceptible to first-pass metabolism in the liver.

Dissolving microneedles are arrays of ultra-small needles made from water-soluble materials typically with lengths in the micrometer range (less than 1000 µm). They create pores in the skin and release drug payload upon microneedle dissolution (dissolving MN).

Dissolving microneedles, mostly using different kinds of Sugars as the matrix , usually release drugs or vaccines quickly in vivo,24 eg, Ito et al25 reported that insulin released from microneedles very quickly, and almost all of the formulated insulin was released within 1 hour when dextrin was used as matrix. Nevertheless, sustained release of drugs or vaccines is also required under some circumstances. Lee et al23 prepared microneedles with model drug encapsulated not within the microneedle tips but only in the backing layer, which served as a controlled-release reservoir that delivered molecules by a combination of swelling the backing with interstitial fluid drawn out of the skin and molecule diffusion into the skin via channels formed by dissolved microneedles. They revealed that Sulforhodamine release from carboxymethyl cellulose microneedle patches exhibited an initial lag time of a few hours, followed by steady release for approximately 1 day. Similar behavior was seen for microneedle patches made of amylopectin, but with slower kinetics. In this case, lag time was

This work is partly presented at 10th World Congress on Pharmacology scheduled during August 02-03, 2018 at, Barcelona, Spain

longer and release took place over a few days. Polymeric dissolving microneedles designed by Donnelly et al have been produced from Gantrez AN-139, and delivered 83% of the encapsulated Kumar et al27 characterized and used maltose microneedles to micro porate full-thickness pig-ear skin to evaluate drug delivery of model small (calcein) and large (human growth hormone) molecules. It was found that modulated theophylline into porcine skin within 24 hours.

Drug Design, Development and Therapy 2013:7submit your manuscript. Dovepress Dovepress948Hong et al transdermal delivery of small as well as large molecules is possible upon micro poration of the skin in combination with iontophoresis (ITP). The modulated ITP protocol resulted in peaks in flux with application of current and gradual decrease with termination of current, and current density and time could be used appropriately to program a desired drug-delivery profile. Garland et al28 studied the potential for ITP to be combined with polymeric microneedle devices that remain in contact with the skin during the course of drug delivery procedure for the first time. Furthermore, it has been shown that the application of an electric current enables the permeation of macromolecules from the entire microneedle-array matrix, and not just that which was contained within the microneedles alone. Thus the application of an electric current significantly increased the extent of macromolecular delivery from the poly(methyl vinyl ether maleic anhydride) microneedle array, which is also promising for the sustained delivery of drugs and vaccines. Wu et al29 reported a similar finding, wherein the transdermal permeation of high-molecular-weight compounds through microneedle-induced channels could be increased through the combination of ITP. Ito et al reported sustained-release self-dissolving micropiles (SDMPs), in which porous silicon dioxide and porous calcium silicate were used as nano porous microparticles to adsorb insulin, and the microparticle-adsorbed insulin was molded to SDMPs using chondroitin sulfate as a base. They concluded that long-acting SDMP preparation would be possible by means of porous silicate adsorbent-held insulin.

Drug Design, Development and Therapy 2013:7submit your manuscript. Dovepress Dovepress948Hong et al transdermal delivery of small also as large molecules is feasible upon micro Poration of the skin together with iontophoresis (ITP). The modulated ITP protocol resulted in peaks in flux with application of current and gradual decrease with termination of current, and current density and time might be used appropriately to program a desired drug-delivery profile. Garland et al28 studied the potential for ITP to be combined with polymeric microneedle devices that remain in contact with the skin during the course of drug delivery procedure for the first time. Furthermore, it's been shown that the appliance of an electrical current enables the permeation of macromolecules from the whole microneedle-array matrix, and not just that which was contained within the microneedles alone. Thus the appliance of an electrical current significantly increased the extent of macromolecular delivery from the Poly(methyl ether maleic anhydride) microneedle array, which is additionally promising for the sustained delivery of drugs and vaccines. Wu et al29 reported a similar finding, wherein the transdermal permeation of high-molecular-weight compounds through microneedle-induced channels might be increased through the mixture of ITP. Ito et al reported sustained-release self-dissolving micropiles (SDMPs), during which porous silica and porous calcium silicate were used as nano porous microparticles to adsorb insulin, and the microparticle-adsorbed insulin was molded to SDMPs using chondroitin sulfate as a base. They concluded that long-acting SDMP preparation would be possible by means of porous silicate adsorbent-held insulin.3

Recent Publications

[1] Gonzalez Garcia, L.E., et al., *Protein Interactions with Nanoengineered Polyoxazoline Surfaces Generated via Plasma Deposition.* Langmuir, 2017. 33(29): p. 7322-7331.

[2] Ramiasa, M.N., et al., *Plasma polymerised polyoxazoline thin films for biomedical applications.* Chemical Communications, 2015. **51**(20): p. 4279-4282.

[3] Macgregor-Ramiasa, M.N., A.A. Cavallaro, and K. Vasilev, *Properties and reactivity of polyoxazoline plasma polymer films.* Journal of Materials Chemistry B, 2015. **3**(30): p. 6327-6337.

[4] Taheri, S., et al., Substrate independent silver nanoparticle based antibacterial coatings. Biomaterials, 2014. 35(16): p. 4601-9.

[5] Cavallaro, A.A., M.N. Macgregor-Ramiasa, and K. Vasilev, Antibiofouling Properties of Plasma-Deposited Oxazoline-Based Thin Films. ACS Applied Materials & Interfaces, 2016. 8(10): p. 6354-6362

Biography

Laura is a second year PhD Engineering student at the Future Industries Institute, UniSA. She is working on the development of biodegradable microneedles arrays for the delivery of viral vaccine vectors and osteoarthritis therapeutics. Her focus is on the use of plasma polymer films for the control of the

Microneedles dissolution and cargo release kinetic, as well as further surface functionalisation with nanoparticles and molecules. Prior to her PhD studies she obtained her MSc in Analytical Chemistry from Bangor University where she worked with pH-responsive polymer coated gold nanoparticles for drug delivery and gene therapy applications

This work is partly presented at 10th World Congress on Pharmacology scheduled during August 02-03, 2018 at, Barcelona, Spain