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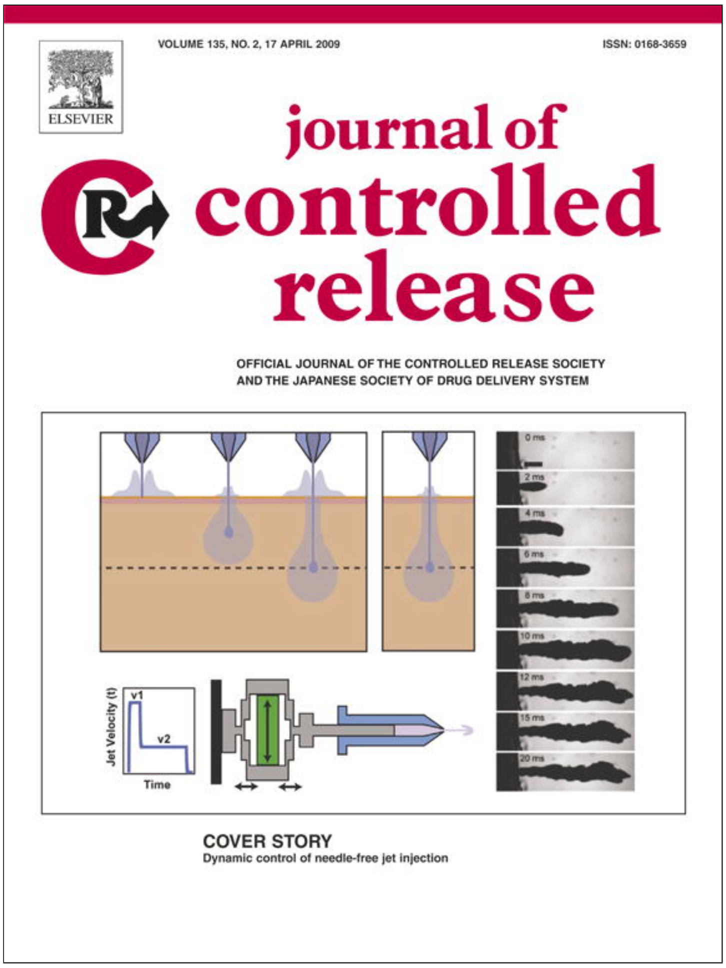

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Journal of Controlled Release 135 (2009) 103

Contents lists available at ScienceDirect

Journal of Controlled Release

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Cover Story

Dynamic control of needle-free jet injection

Needle-free devices for transdermal drug delivery are of growing interest to those who give injections as well as to those who receive them. Needle-free drug delivery has the potential to improve comfort and compliance for many who require frequent injections, such as type I diabetics. It can also make vaccinations safe and affordable in many places in the world, e.g., the developing world where disposable needles and syringes are cost prohibitive and often pose safety risks. Jet injection, a popular means of needle-free delivery, employs compressed gasses or springs to generate high-speed liquid jets that penetrate the skin and deliver drugs. While these devices have had some success in the marketplace, they have not gained wide acceptance due to reportedly painful injections and lack of reliability in the amount of drug delivered and the depth of skin penetration. The skin poses a significant challenge to jet injectors because it has a complex mechanical structure in which the outermost layers have the greatest density and strength. Further, skin properties vary greatly between individuals, across different regions of the body, and with changes in environmental conditions such as humidity. The poor performance of conventional jet injectors, which use a roughly constant jet velocity, arises at least partially from the difficulty of addressing this complexity and variability with springs and compressed gasses.

Over the last few years, the laboratories of Professor Daniel Fletcher at University of California-Berkeley and Professor Samir Mitragotri at University of California-Santa Barbara have been working together to improve the performance of these devices. Using precisely controlled piezoelectric actuators, the same technology used in many inkjet printers, these groups have designed and tested novel injector prototypes that improve understanding and control of the complex jet–skin interactions [1,2]. In this issue, Stachowiak et al. report a dynamically controlled jet injection device which provides a significant step towards improved transdermal jet injectors [3]. This device uses a mechanically amplified piezoelectric actuator to vary the velocity of a fluid jet in real-time, achieving greater control of skin–jet interaction and penetration depth. Based on a computational model of the piezoelectrically-actuated jet injector, the authors have designed a jet velocity "profile" in which the jet velocity is initially high and is subsequently reduced to a lower level. The initial period of high jet velocity is used to define the depth at which the drug is delivered, and once the desired depth is reached, the jet velocity is reduced so that a controlled drug dose can be delivered without the risk of drug overflow and splash-back. In this way, the "depth definition" and "dose delivery" functions of the needle-free device are decoupled, facilitating greater control and reliability. One of the significant findings by the authors is that adjusting the proportion of the injection volume delivered at high speed can precisely control penetration depth in tissue model materials. Experiments on human skin suggest that the efficiency of jet injections can be optimized by the use of dynamic control through reduction of splash-back from the skin surface. This work demonstrates that control of jet velocity has the potential to significantly improve the reliability of jet-based transdermal drug delivery. It is also expected to drive the development of other liquid jet-based devices [4]. A fresh perspective on jet-based transdermal injections by Professors Fletcher and Mitragotri is expected to inspire more effective commercial devices benefiting all of us.

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0168-3659/$ – see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.jconrel.2009.03.001