A new screening in-vitro method to study drug release in early development of transdermal drug delivery systems

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INTRODUCTION: Dissolution is the required characterization test to evaluate new materials for transdermal drug delivery [1]. However the conventional dissolution tests, recommended by United State Pharmacopeia (USP), cannot provide results with good correlation with in vivo drug release, especially for patches that mainly depends on skin resistance to drug diffusion [2]. Other dissolution methods, such as Franz diffusion cell, horizontal permeation system and flow-through diffusion cell, can provide skin resistance and penetration effects and are commonly used to study skin permeation assay [3]. However, these tests are costly and the swelling of stratum corneum increases penetration and uptake of drug [4]. The purpose of this study was to develop a novel, selective and easy-to-handle in vitro method, which could better than the USP method imitate the diffusion and moisture level of skin. Further, this method can be especially helpful to study the drug release profiles of different transdermal formulations in early development.

METHODS: Durogesic patches of two strengths (12 and 75 µg/hr) were used as model transdermal devices in all experiments. One patch was placed on a piece of synthetic skin simulator (SSS) (2×2.5cm² or 5.5×6 cm²) that was wetted with pH 6.8 buffer (300µl or 1800µl). The patch and simulator were wrapped and fixed on flat surfaces to minimize the evaporation and displacement. The patch was moved to a new wetted SSS, while the former piece was collected and soaked in pH1.0 buffer for 3 hours for complete extraction. The concentrations of fentanyl were analyzed by HPLC with UV detector in triplicates. Data was plotted as the cumulative amount of drug released as a function of time. For comparison, the patches were also tested with the standard USP dissolution bath (Sotax AT7 Smart, Sotax AG, Switzerland) equipped with mini vessels and paddles. The dissolution tests were taken place in phosphate buffer with pH 6.8 and the concentrations were measured in duplicates.

RESULTS: Durogesic patch is a controlled release transdermal device, which could release fentanyl drug at constant rate for three days. As shown in figure 1, Durogesic patches of both dosing strengths released over 90% of drug within 6 hours by the USP method. The drug release profile obtained by the SSS method was more comparable with the stated clinical release. The standard deviation (denoted as error bars in figure 1) indicated that the SSS method had small variations between the measurements of the drug release from the patches.

DISCUSSION & CONCLUSIONS: The experiment showed that the new in vitro testing method could provide significantly more comparable dissolution profile to the in vivo uptake than the USP method. This simple method could be particularly helpful to select appropriate formulations for transdermal patches in early development.


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Figure 1. Drug release profiles of durogesic patches (12 and 75µ/hr) measured by USP and SSS methods were compared with the stated clinical release.