Dissolution of Poorly Soluble Drug Nanoparticles from Edible Polymer Stripfilms

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ABSTRACT SUMMARY

The dissolution of poorly soluble active pharmaceutical ingredients (API) from stripfilm composed of edible polymer matrix was characterized using a novel in-situ Surface Dissolution Imaging (SDI) system (Sirius, US), which is an Ultraviolet (UV) based platform. In contrast to dissolution tests using USP IV, which may not be able to discriminate drug dissolution from nanoparticles vs. micron-sized drug particles, SDI system allowed discernment based on effective intrinsic dissolution rates.

INTRODUCTION

A simple, potentially continuous process of incorporating nano-sized and micron-sized drug particles of poorly water-soluble drugs, more specifically, the Biopharmaceutical Classification System (BCS) Class II drugs, into edible polymer films as a versatile dosage platform has been recently developed¹. Thin stripfilms exhibited enhanced dissolution rates resulting in an immediate release of poorly water-soluble drugs. Depending on the thickness and the matrix, such film format is also amenable to sustained release of BCS Class II drugs; e.g., drug release taking over 15 h from a 2000 micron thick film.

Wet stirred media milling (WSMM) has been shown to easily produce 150 to 2000 nm stable drug particle suspensions². Such particles may be embedded into films to potentially alter the dissolution profiles. Interestingly, however, even from a relatively thin film of about 60–100 microns, it is not possible to discern the dissolution profiles of 150 and 500 nm drug particles using an USP apparatus, since the drug release is matrix erosion limited. Clearly, for the purpose of stripfilm based drug product development, it is necessary to better understand the actual release rate of drug from the particles embedded in the stripfilm. Consequently, in this work, UV detection based Surface Dissolution Imaging (SDI) system was used to assess dissolution rates from films consisting of different sizes of particles to discern the impact of particle size on dissolution performance.

EXPERIMENTAL METHODS

The general protocols of WSMM and film preparation have been reported elsewhere¹,². Here, griseofulvin (GF) was selected as a model BCS Class II drug. The suspension was milled as 8.8% w/w GF, 2.2% w/w pullulan, 0.2% w/w SDS and 88.8% w/w DI water. The GF particle size was characterized using laser diffraction (Coulter LS3320, Beckman, US), and d50 of 150 nm, 500 nm and 14 micron were achieved through milling for 90 min, 6 min and 0 min, respectively. The polymer solution consisted of 19.9% w/w pullulan, 3.3% w/w glycerin, 0.3% w/w Gum and 76.5% w/w water. The suspension and polymer solution were mixed in at a proportion of 1/0.28 w/w for 6 h, and then cast on a PET substrate for drying. The GF concentration in the dry stripfilm was quantified by UV-spectroscopy (SOTAX, USA) as 9%. For dissolution imaging, round samples (ID: 3/8") were punched from dry films. For comparison study, the placebo (film without API) and the tablet pressed using as-received GF were also used. The dissolution conditions were manipulated by flowrate of DI water consisting of 4 stages, i.e. nominal fasted flowrate (0.2 mL/min for 10 min), nominal fed flowrate (0.8 mL/min for 10 min), quick flush (2 mL/min for 1 min) and static (0 mL/min for 6 min) simulation. Each simulation was at 37 °C and lasted for 27 min in total, and 280 nm wavelength was used for monitoring the GF during the simulation. Intrinsic dissolution rate (IDR) was estimated as the dissolution rate per area (mg/min/cm²) and was selected for characterizing the drug release behavior,
whereas the UV images were captured to quantify the mass of GF released from stripfilm during the dissolution.

RESULTS AND DISCUSSION
The IDR results of stripfilms with different particle size are given in Figure 1.

![Figure 1. IDR results for films embedded with three different sized GF particles](image)

The small particles showed better IDR performance, especially for the 150 nm particles which generated greater IDR than other three samples under the high flow rate. This is in contrast to the USP tests that cannot show any discernment between 150 and 500 nm particles. Overall, these results suggest use of very fine particles of BCS Class II drugs is justified for both immediate and sustained release applications. The snapshots of GF release from different samples were captured at the same time point (14 min), and the results are given in Figure 2. Fast release from 150 nm particles is evident, corroborating the IDR results.

CONCLUSION
The dissolution of GF from different particle sizes contained in edible polymer stripfilms was successfully visualized using a novel in-situ SDI system. The results indicate that stripfilms provide a promising platform for delivery of poorly water-soluble drugs and the use of smaller particles is advantageous for very quick drug release. The results suggest that stripfilm embedded with nano-particles could be used for immediate as well as stable sustained API release.

![Figure 2. GF release at 14 min, the concentration of GF is indicated by warm color.](image)

REFERENCES

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