A Connected Workflow to Streamline Tablet Manufacture and Dissolution Testing

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1. Introduction

Current practices for developing new drug products that have adequate safety and quality profiles are fragmented, costly and inefficient process. Typical workflows involve siloed laboratories. Tablets are manufactured in one laboratory or facility and then transferred often across departments to another for analytical testing. Automation and the adoption of industrial digital technologies have the potential to significantly accelerate drug development while improving resource efficiency and productivity, especially in a development phase that faces increasing pressure.

To address these fragmented workflows, we connected a self-driving tablet manufacturing system and a fully automated dissolution system. The connected workflows were then used to evaluate 2 grades of ibuprofen (25 D_{50}= 20-33µm and 50 D_{50}= 45-60µm; varying particle size), with different percentages of croscarmellose sodium levels as disintegrant (2%, 5% and 8%). Six formulations were prepared using microcrystalline cellulose and lactose as fillers at fixed ratios (adjusted to accommodate the varying disintegrant levels) and 1% magnesium stearate as lubricant. Each blend was directly compressed into tablets to achieve target porosities of 10%, 15% and 20%.

This large dataset enables a deeper understanding of the multifactorial effects of drug particle size, formulation variables, and process conditions on tablet drug release. The results indicate that ibuprofen particle size (across different grades) and disintegrant concentration are the primary factors influencing dissolution time. In addition to expanding the understanding of how different ibuprofen grades and disintegrant levels impact dissolution performance, this study also demonstrated the dramatic gain in time efficiency. Tablet manufacture and dissolution testing were completed in just under 57 continuous hours compared to approximately three working weeks when performed manually.

By integrating the two systems (a real-time dissolution measurement platform and a self-driving tablet manufacture) a feedback loop can be established to enable continuous evaluation and adjustment of formulations against predefined dissolution targets. This has the potential to transform timelines for the development of formulation and process conditions to deliver high quality drug products that meet manufacturability and performance targets.

2. Figures and tables

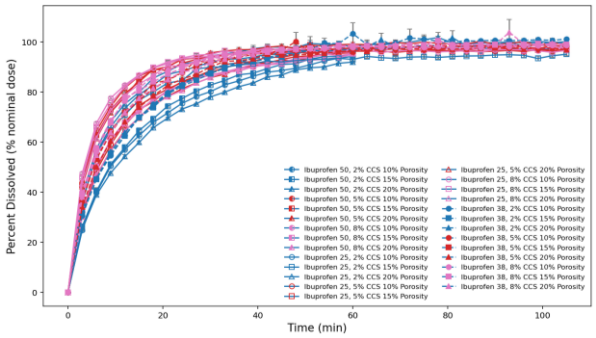

Fig. 1: The dissolution profiles (percent dissolved %nominal dose). Each formulation comprised of 10% Drug Loading Ibuprofen of varying particle size (D_{50}); for each curve n= 6.

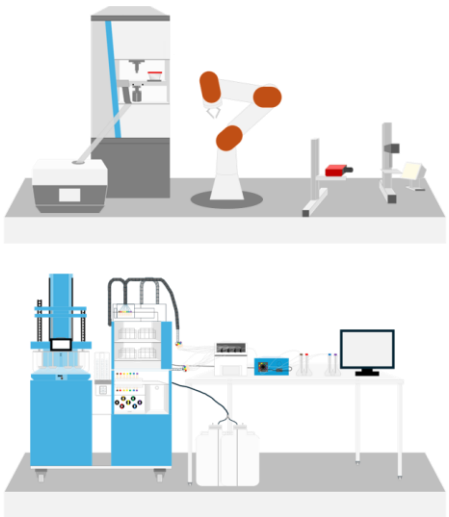

Fig. 1: (Top) Self-Driving Tablet Manufacture comprising of compaction simulator, tablet tester and sessile drop (Bottom) Fully Automated Dissolution System, comprising of dissolution baths and online-UV.
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