Additive Manufacturing and Characterization of Mini-Devices for Oral Drug Delivery - DTU Orbit (23/10/2019)

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The complex nature of the human gastro-intestinal system, by the presence of digestive enzymes, harsh changes in pH, presence of thick mucus layers, etc., often accounts for low bioavailability of orally ingested drugs. In contrast to alternative routes of drug administration, the oral route is preferred, due to a combination of simplicity, safety and patient compliance. Hence, many strategies for increasing bioavailability of orally administered drugs have been developed within the pharmaceutical and related research areas. Among those is the application of drug transporting and protecting delivery platforms, which include engineered microdevices featuring a reservoir and consequent unidirectional drug release. These devices have been a subject of intensive research since almost two decades and have been shown potent as universal carrier platforms with promising oral drug delivery performance. While the fabrication of microdevices could be demonstrated by means of various fabrication protocols with different materials, it remained largely associated with elaborated and costly microfabrication techniques with limited capacity for geometrical complexity.

In this Ph.D. thesis, the implementation of additive manufacturing (3D printing) as an alternative fabrication method with increased simplicity, cost-efficiency and geometrical design freedom is demonstrated and evaluated. Within the frame of a feasibility study, the process of using state-of-the-art micro stereolithography additive manufacturing was thoroughly characterized and associated limitations and opportunities were unveiled. A laser spot size of 30 µm, limiting the fabrication of microdevices to millimeter scale, and the lack of the possibility to fabricate individual releasable devices, were found to be the main challenges.

The implementation of pre-fabricated sacrificial release substrates in photopolymerization-based digital light processing additive manufacturing has been realized and it enabled the fabrication of patterns of delicate microstructures and their subsequent release. Using those sacrificial release substrates for the fabrication of microdevices for oral drug delivery allows additive manufacturing to be fully integrated into potential workflows of microdevice fabrication in which various processing steps, such as drug loading and coating, are connected. Microdevices were fabricated on sacrificial release substrates and were successfully released. The rapid prototyping potential of additive manufacturing was employed to fabricate devices with alternative geometries with the aim of improving oral drug delivery performance. Characterization of different designs with use of a retention model showed that distinct surface structures led to an enhancement of mucoadhesion, while favorizing the reservoir-containing side to the intestinal wall, thus indicating a potential for their self-orientation.

Finally, the used retention model has been improved for increased physiological relevance and experimental reproducibility. A fully integrated instrumentation based on open labware and a detailed corresponding documentation for simple replication using rapid prototyping techniques such as additive manufacturing and CO2 laser cutting have been developed.

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