The development of flow-through dissolution method for injectable silica-based drug delivery formulations

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Introduction

Silica (silicon dioxide, SiO_2) is a biocompatible and a nontoxic material which has a GRAS (generally regarded as safe) status. In the controlled drug delivery systems, biodegradable silica products has been used as a matrix material to deliver drugs especially by parenteral dosing. An increasing number of new drugs developed are chemically unstable and cannot be administered orally such as proteins and peptides. Biodegradable sol–gel derived silica matrices can be used to encapsulate different kinds of biologically active agents like small drug molecules, proteins, and viruses (Fig. 1).

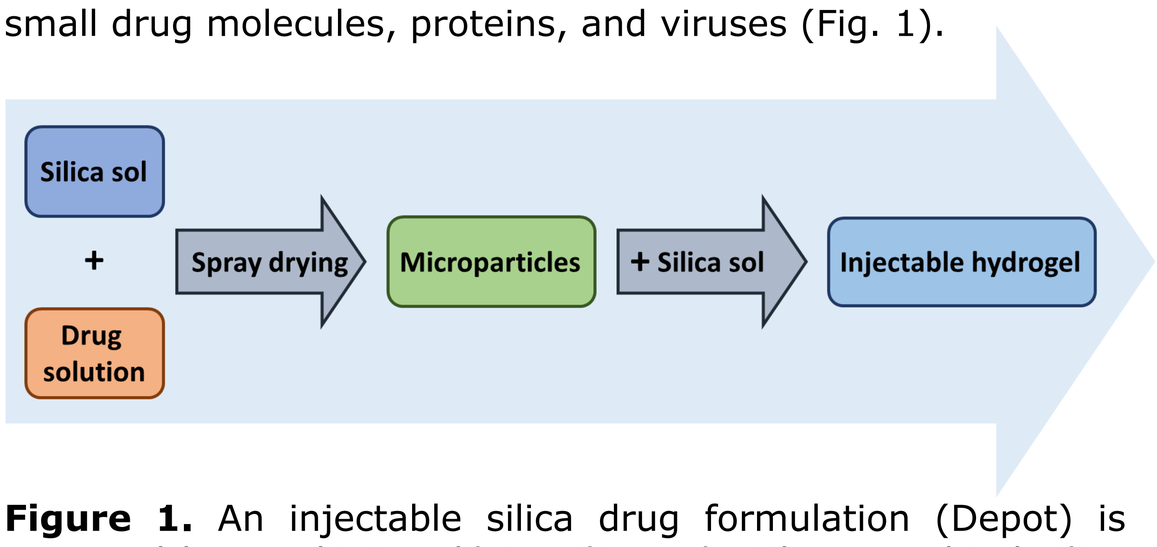

Figure 1. An injectable silica drug formulation (Depot) is prepared by combining dilute silica sol with spray-dried silica microparticles with encapsuled drug.

In vitro dissolution testing is an important analytical tool that is used to investigate drug release rate. The continuous flow method is the best method to simulate the dynamic *in vivo* environment of the subcutaneous tissue. Characterization of the drug release from long-term dosage forms is important to ensure product quality and performance.

The aims of the study

The aim of the master's thesis work is to assemble and test a flow-through dissolution system which especially mimics dissolution of the drug in subcutaneous *in vivo* environment. The developed *in vitro* dissolution method is tested with injectable silica dosage form developed by DelSiTech Ltd.

Methods

Dissolution samples were analysed in defined time intervals for drug (HPLC) and silica (spectrophotometric method). The optimized flow-through dissolution method prototype is tested with a fast and a slow releasing injectable silica formulation. These results are compared with sample and separate dissolution method, and with *in vivo* data of subcutaneously injected test formulations.

Results

The flow-through dissolution method was modified and optimized to achieve conditions that resemble subcutaneous environment by adjusting parameters like flow rate, buffer, and temperature (Fig. 2). Fresh physiological buffer continuously passes through the flow-cell containing the drug-loaded depot and collected samples are analysed.

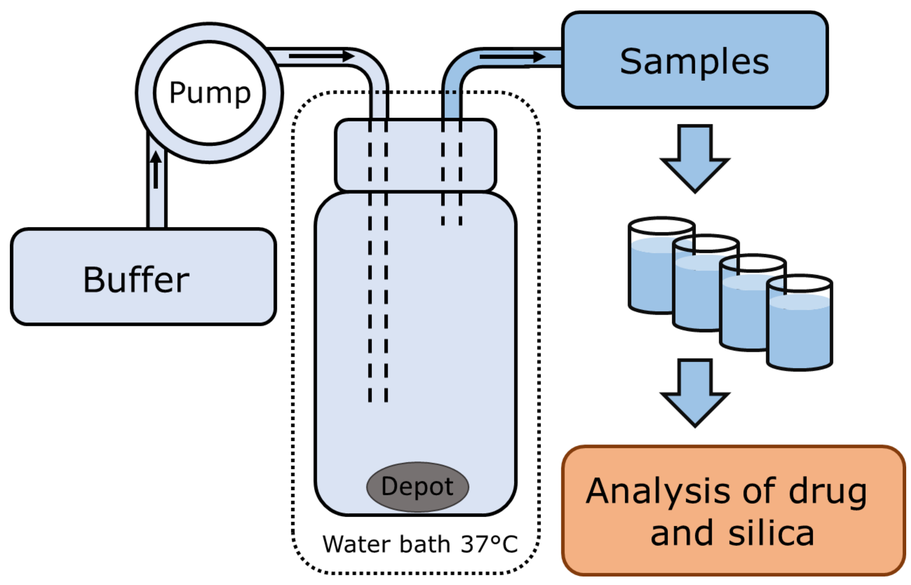

Figure 2. The flow-through dissolution system (not in scale).

The analysed samples from sample and separate method and from optimized flow-through dissolution method show that the sample and separate method is approximately 10 fold faster than flow-through method (Fig. 3).

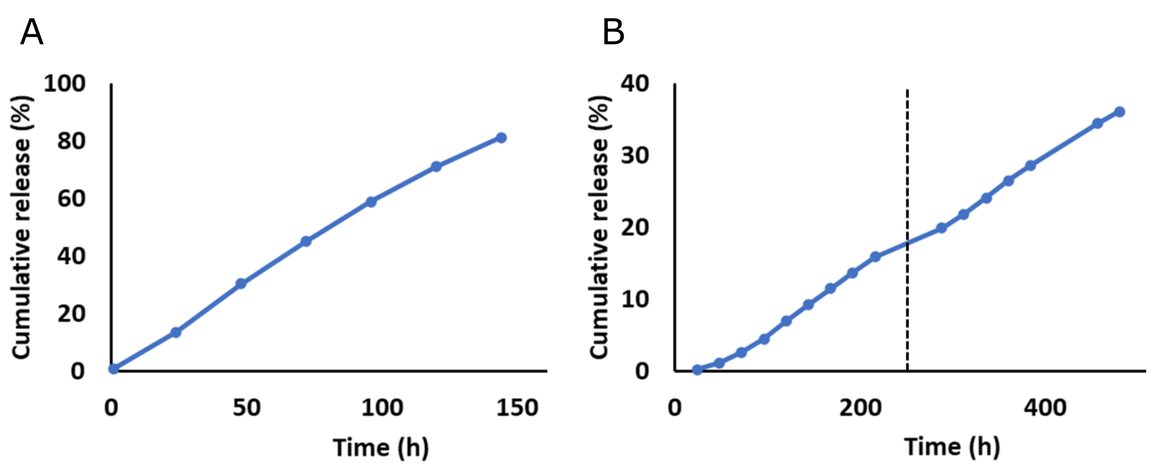

Figure 3. The cumulative degradation of silica tested with sample and separate method (A) and tested with flow-through dissolution method (B).

Conclusions and future plans

The flow-through method is working and can be used for testing injectable silica-based drug formulations. To ensure that the flow-through dissolution method works, it will be tested with a test drug encapsulated in a fast and a slow releasing injectable silica formulation. Furthermore, these results are compared with *in vivo* results to confirm *in vivo* relevance.