# Electroencapsulation of Mesoporous Silicon Particles for Controlled Oral Drug Delivery

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*Abstract—Mesoporous silicon* (*PSi*) has lately been the focus of interest as a potential new orally dosed drug carrier in a steeply increasing number of papers, where the strengths of PSi in such applications has been shown. Perhaps most importantly, drugs will remain in an amorphous form instead of crystallizing while loaded into the pores of PSi. The advantage of this is greatly increased solubility and dissolution rate of the drug. In the present work, we investigate the possibility of enhancing the drug carrier functionality of PSi micro- and nanoparticles by encapsulating the drug loaded PSi particles in a suitable polymer capsule structure by the method of collision of oppositely charged, electrosprayed droplets. Embedding the PSi particles in such polymer structure of micrometer scale will not only vastly improve the workability of PSi nanoparticles and the smallest of microparticles, but with suitable material choices will also potentially enable targeted release of the drug loaded PSi particles to a desired part of the gastrointestinal (GI) tract. This would help towards eliminating the intestinal first-pass effect of an orally dosed drug, which together with the already advantageous properties of PSi would result in an increased bioavailability of the drug. The gained advantage would be significant, since it has been estimated that more than 95% of new drug candidates suffer from poor pharmacokinetic properties, resulting in poor bioavailability.

## I. INTRODUCTION

Where possible, the oral route is often preferred for drug administration due to comfort of usage and a well controlled drug release rate. However, many potential drug molecules possess poor pharmacokinetic properties, such as poor solubility, dissolution of the drug in the intestinal lumen, poor permeation in the gastrointestinal (GI) tract, or high intestinal or hepatic first pass metabolism. Hence the bioavailability of the drug will be inadequate when administered orally, resulting in poor efficiency [1]-[4].

During the past decade, the strengths of *mesoporous silicon* (*PSi*) as a potential drug carrier medium have been shown. Drugs confined to the pores of PSi will not form crystal lattices as easily as free drug molecules, but instead remain to some extent in its amor-

phous form. This has a significant effect on th e solubility and the dissolution rate of the drug in the intestinal lumen. The drug release rate is easily adjustable by changing pore properties. Drugs can be l oaded to the pores of PSi particles in room temperature solvents, enabling the usage of temperature sensitive drugs such as peptides and hormones [1], [5]-[7].

This presentation discusses the electroencapsulation of drug loaded PSi particles in order to enhance the oral drug delivery process. Such composite capsule particles possess the shielding properties of the selected capsule material and good workability of the drug due to the achieved greater size scale of the processed unit. After the capsule shell layer dissolution in the GI tract, the drug release rate will b e completely determined by the properties of the released drug loaded PSi particles. The structure potentially enables safe delivery and controlled release of drug l oaded PSi particles in a selected part of the GI tract when dosed orally [8], [9].

## II. MATERIALS AND METHOD

### A. Electroencapsulation setup

The PSi particles are encapsulated by the means of electrospraying. The used setup is shown schematically in Fig. 1. Two streams of micro-size droplets consisting of two mutually immiscible but wettable liquids, a shell liquid and a core liquid, are electrosprayed in cone-jet mode from two nozzles kept at oppositely signed electric potentials. As a result, the droplets in each stream become charged in opposite signs and connect inside the electrospraying chamber due to Coulomb attraction. By adjusting the volume flow rate, applied voltage and inner diameter of each nozzle according to the material choices, the process can be stabilized while bringing the mean droplet size and charge per droplet ratio of the two electrosprays sufficiently close to each other to enable formation of complete microcapsules that are electrically neutral. A capsule is formed as a shell liquid droplet (of a lower surface tension than that of the core liquid droplets) envelope a core liquid droplet upon impact. The shell solvent then evaporates, leaving behind a solid shell layer. Neutralized capsules are easily collectable as they fall to the bottom of the chamber. The temperature and pressure of the electrospraying chamber can be adjusted to optimize the evaporation rate of the used solvents so that the evaporation will occur only after droplet combination, but before the formed capsules reach the bottom of the electrospraying chamber.

The setup consists of two conductive capillaries angled 30 degrees with respect to each other, which are run through an insulating air-tight lid into a heatable vacuum chamber (inner diameter 110 mm, inner height 840 mm). The electric potential of each capillary is oppositely signed and independently adjustable. The vacuum chamber walls and ground plates suspended from the capillary constructs are grounded. The nozzle tips are changeable to enable the usage of different nozzle inner diameters (ranging from 0.10 mm upward). The position of the nozzle tip relative to the capillary construct lower (high voltage) surface and to the freely movable ground plate are adjustable. Volume flow rates through each nozzle are programmable, and sprayed particles can be collected in a dry Petri dish or in a gelatinizing path to enhance the capsule shell hardening, in case normal pressure is used. A LED lighting system and two specially constructed windows (not

visible in Fig. 1.) are posi tioned below the lowest level of the ground plates' freedom of action to provide a possibility to observe the electrospraying process visually.
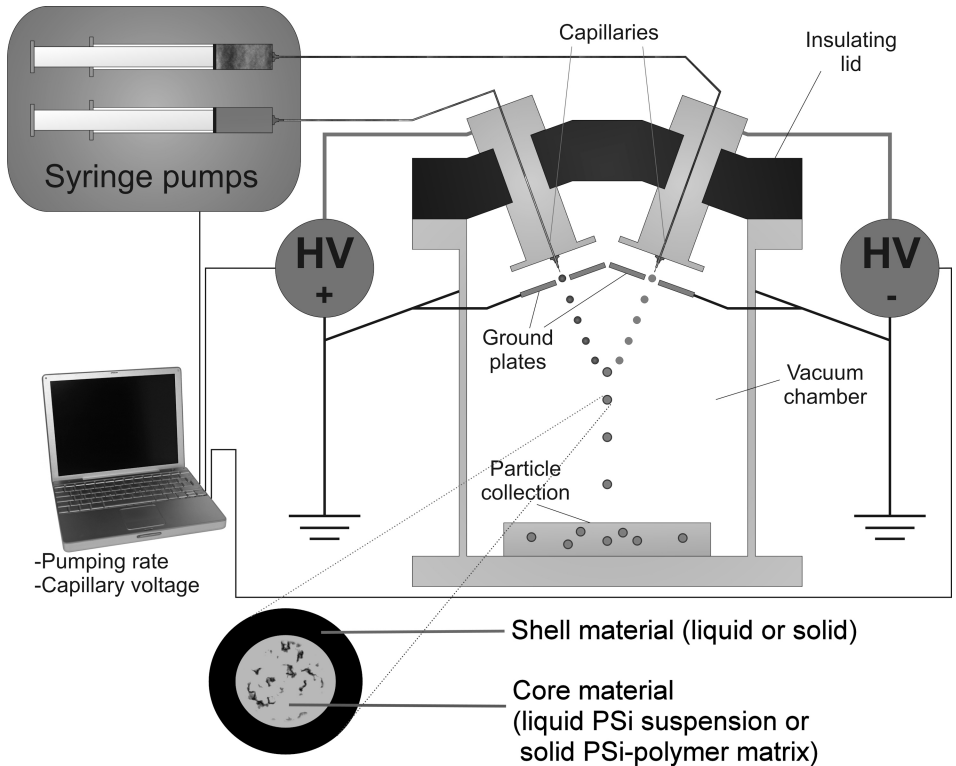


Fig. 1. A schem atic diagram of the used electrospra ying set-up. The illustrated electrospraying chamber is greatly flattened for clarity of the diagram.

### B. Materials

For th e d emonstrative cap sules p resented in th is p aper, Eudragit® E 100 pol ymer shel l was used. The electrosprayed shell liquid wa s com posed of t he pol ymer di ssolved i n chloroform, with concentrations ranging from 200 to 300 mg/ml. Less than 10 mg/ml of talc was added to reduce adhesion o f cap sules to th e b ottom o f th e p article co llection dish. The capsule core l iquid was a suspensi on of PSi microparticles in glycerol, doped with about 0.03 M of NaI t o improve conductivity and l ess than 1 m g/ml of fl uorescein to facilitate detection of cap sule leakage. The PSi particles were therm ally carbonized, and sieved using a 25 µm sieve. Concentration of PSi in glycerol was 10 mg/ml.

### C. Microcapsule production by collision of two oppositely charged electrosprays

The experimental microcapsules produced for t his paper were el ectrosprayed in normal air pressure. The interior of the electrospra ying chamber was held at a tem perature of 35 °C. The shell liquid was kept at 25 °C immediately before feeding the liquid through the electrospraying chamber lid, while the gl ycerol based core l iquid was heat ed t o 42 °C.

The slightly increased temperature decreases the viscosity of glycerol considerably, and this together with the increased conductivity due to NaI-doping and reduced volume flow rate (discussed later) helped to stabilize the atomization process of glycerol and decrease the attained droplet size. On the other hand, excessive heating would have resulted in premature evaporation of chloroform from the atomized shell liquid droplets.

For both nozzle systems, the distance between the circular lower surface of the capillary construct and the suspended parallel circular ground plate, both 32 mm in diameter, was 9.0 mm. Diameter of the center holes in the capillary construct and ground plate were 5.0 mm and 12.0 mm, respectively. The nozzle emerged out of the center hole of the upper plate surface, with the tip lying close to the center of the volume between the parallel plates.

With the used temperatures and geometry, nozzle voltages of -2.9 kV and +5.3 kV were used to induce the cone-jet modes for shell and core liquid atomization, respectively. Volume flow rates of 2.50 ml/h and 0.75 ml/h were used, respectively, to even out the attained mean droplet size.

The inner diameter of the used nozzles affects the stability of the electrospraying process, and possibly contributes slightly the observed mean droplet size. While fine nozzles are preferable to achieve a stable process and the smallest possible droplet size, the electrosprayed liquids and the used conditions dictate the minimum limit for the inner diameter of the nozzles used. Narrow capillaries will quickly get clogged by precipitations of the sprayed polymer solutions if the evaporation rate of the used solvent becomes too high because of raised temperature of high voltage. While using PSi suspensions, agglomerates of PSi particles will quickly form to the capillaries if the maximum particle size is too close to the inner diameter of the used capillary. Too wide capillaries may cause problems in stability, as the volume of the induced Taylor cone increases within an intense, inhomogeneous electric field. In the present work, nozzles of inner diameter of 0.41mm were used.

Using the defined parameters, a stable encapsulation process was achieved and a sample of capsules was collected at the bottom of the electrospraying chamber on a dry Petri dish.

### III. Results and Discussion

Encapsulation of PSi particles by the method of dual nozzle electrospraying seems successful, based on visual observation. Microscope images of some of the collected capsules after ten days of storage in a temperature of 22 °C and relative humidity of 23 % are shown in Fig. 2. The largest PSi particles can be spotted as dark areas through the partially invisible capsule shell layers. The capsules are easily detachable from the collection dish, and can be moved around without glycerol leakages. Pressure durability measurements are necessary to investigate the feasibility of the capsules for tablet pressing.

The produced capsules are close to monodisperse, with a mean size of about 30-40 μm. The observed mean size is a good balance for fast dissolution of the capsule shell layer in triggering conditions and, on the other hand, easy workability of the capsules. By earlier experiments we can conclude that using PSi particles smaller than 25 μm of mean size (e.g. nanoparticles) in the core liquid does not alter the structure of the produced

capsules in any significant way. However, us      age o f larg er th an 2 5 µm  PSi p  articles quickly leads to structural problem s, as in su ch a scenario the PSi pa rticles can be larger than the mean size of an electrosprayed core liquid droplet.
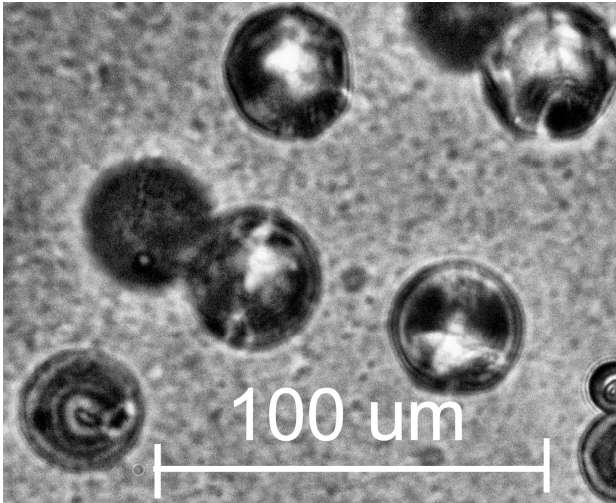


Fig. 2. Microscope image of produced Eudragit® E 100-glycerol-Psi capsules.

The next step in our work is manufacturing capsules of an enteric polymer shell, filled with drug loaded PSi micro- or nanoparticles to enable controlled drug release in the selected part of the GI tract.    This will  involve encapsulation expe riments using new solvents and base liquids for the capsule core suspension, followed by *in vitro* drug dissolution measurements and tabletization experiments.

Should the electroencapsulation m ethod prove  useful for ultim ately helping im prove the bioavailability of poorly soluble drugs in   oral dosing, a scale-up in capsule production rate will be required for industrial applica tions. For scientific experim ents, the yield of a single dual nozzle electrospraying system is adequate.

## IV. ACKNOWLEDGMENTS

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