## Poster 7

# SOL-GEL MICROSPHERES AND NANOSPHERES FOR CONTROLLED RELEASE APPLICATIONS

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## ABSTRACT SUMMARY

We present a novel approach to the synthesis of inorganic sol-gel microspheres for encapsulating organic and bioactive molecules, and controlling their subsequent release kinetics. The bioactive species are incorporated, at ambient temperature, into the inorganic particles using an emulsion gelation process. Independent control of the release rate (by adapting the nanostructure of the internal pore network to the physico-chemical properties of the bioactive molecules) and particle size (by tailoring the emulsion chemistry) is demonstrated.

**Keywords:** ceramics, encapsulation, inorganic gels, hydrophilic matrices, microspheres

## INTRODUCTION

Sol-gel chemistry has been shown to be a flexible technique for producing inorganic silica matrices with tailored microstructures, which can be used for the encapsulation and controlled release of organic and bioactive molecules. The present paper extends this concept by combining sol-gel chemistry with an emulsion approach for producing inorganic particles with controlled dimensions, and demonstrates how the particle size and microstructure can be independently controlled.

## EXPERIMENTAL METHODS

*Sol-Gel Chemistry and Encapsulation of Model Compounds*. A stock solution of 4-(2-hydroxy-1-naphthylazo) benzene sulfonic acid (*Orange II*) was produced by dissolving *Orange II* in water (0.1 wt%), and adjusting the pH to the required value. Sol-gel solutions were subsequently prepared by mixing the aqueous solution with tetramethylorthosilicate (TMOS) and methanol (MeOH), to achieve $H_2O$:TMOS (*W*) and MeOH:TMOS mole ratios (*D*) of four. The resulting solution was stirred and left to age at ambient temperature for one day.

A transparent emulsion was prepared by mixing selected surfactants and organic solvents. The surfactants used included sorbitan monooleate, sorbitan monolaurate and bis-2-ethylhexylsulfo-succinate (AOT), while the organic phase was typically chosen from the group consisting of kerosene, hexane, heptane, octane, decane, dodecane and cyclohexane. The sol-gel solution was added to the emulsion, and the resulting mixture was stirred at 500 rpm for one hour. The particles thus produced were washed with cyclohexane and carefully dried.

*Release Kinetics*. The release of the encapsulated species from the particles was monitored by placing a fixed quantity of the sample in water or physiological saline, and monitoring the concentration of the released species using UV/Vis spectroscopy. The fraction released was normalised to the total mass initially encapsulated.

## RESULTS AND DISCUSSION

1. Influence of emulsion chemistry on particle size.

The influence of the emulsion chemistry on the size of the microspheres obtained at pH 2 is illustrated in Figure 1 for microspheres containing encapsulated *Orange II*. Using essentially identical sol-gel chemistries, particles with dimensions ranging from 50 nm to 50 µm can be readily obtained.

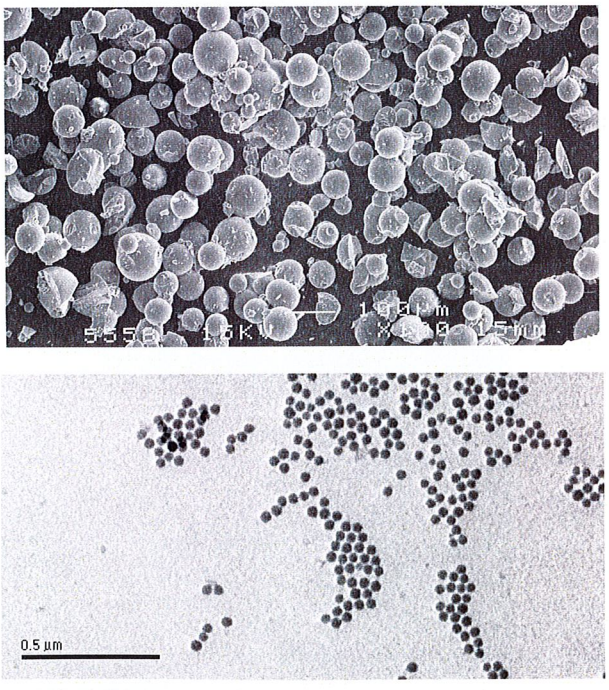
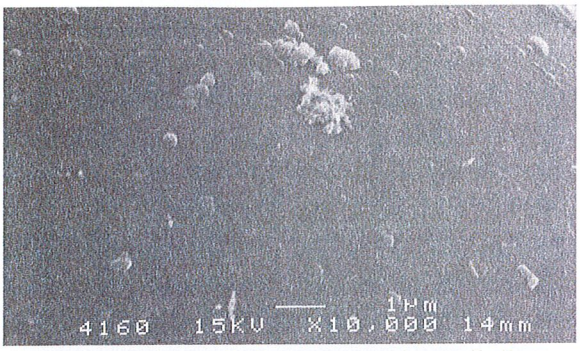
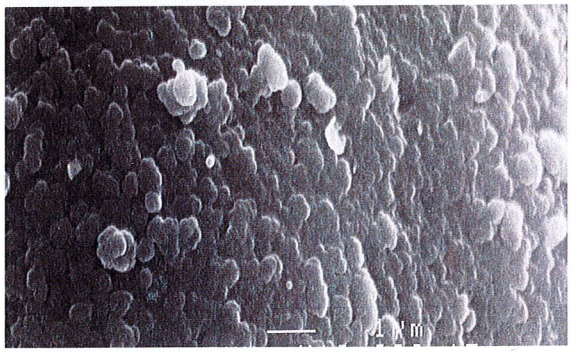



**Figure 1**: Encapsulation of *Orange II* in silica sol-gel nanospheres and microspheres obtained using heptane/sorbitan monooleate (**TOP**) and cyclohexane/NP9 (**BOTTOM**).

The size of the particles is controlled by the size of the emulsion droplets, which act as micro-reactors for the sol-gel reactions. In turn, the size of the droplets is determined predominantly by the hydrophile/lipophile balance of the surfactant/ solvent couple and by processing parameters such as the water to surfactant ratio and the concentration of surfactant.



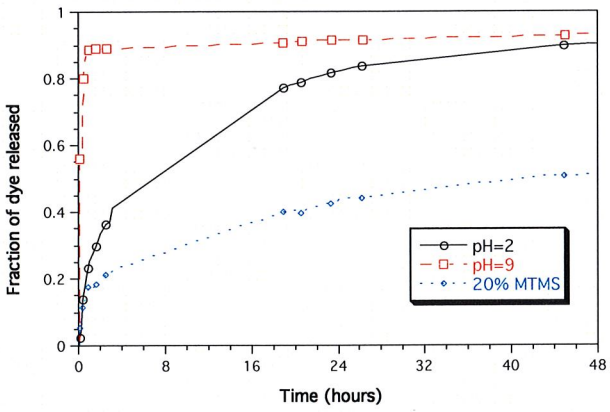




**Figure 2**: Effect of sol-gel synthesis conditions on the microstructure and release kinetics. Samples illustrated in the **TOP** and **BOTTOM** micrographs were prepared at pH 2 and 11, respectively, using sorbitan monooleate and kerosene. The corresponding kinetics for the release of encapsulated *Orange II* are shown in the **BOTTOM** traces.

2. Influence of Sol-Gel Solution Chemistry on Release Rates.

The effect of sol-gel processing parameters on the morphology and associated release kinetics is illustrated in Figure 2. Although both samples have essentially identical particle sizes (not shown), their morphologies are significantly different. Processing under acidic conditions leads to the formation of nanosized linear silicate "building block" which are woven tightly together in the final gel matrix, to produce a microporous material (pore diameters $< 2$ nm). In contrast, three-dimensional fundamental particles are produced under basic conditions, leading to the formation of mesoporous gels (pore diameters $> 2$ nm). The different morphologies are clearly reflected in the release rate of the encapsulated species from the respective matrices; rapid release kinetics are evident for the mesoporous material (high pH), while significantly slower release rates are obtained for the microporous material (low pH).

## CONCLUSIONS

A combined sol-gel/emulsion processing method has been developed to produce inorganic matrices with tailored nanostructures containing encapsulated organic and bioactive molecules. Control of the release kinetics is achieved by tailoring the internal nanostructure of the matrix during synthesis and encapsulation, while the particle size of the matrices is controlled through the emulsion chemistry. This approach enables the size and internal structure of the matrices to be independently controlled. The wide range of particle size (from nanometers to microns), combined with the potential to control the release kinetics independently from the particle size, make this technology very attractive for a wide range of therapeutic applications.

## REFERENCES

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