

Drug Release and Spectroscopic Examination of an Ion Exchange Resin

Thomas M Breunig, Harlan S Hall, J Scott Madsen
Coating Place, Inc, PO Box 930310, Verona, WI 53593
tombreunig@encap.com

ABSTRACT:

The performance of an Ethylcellulose coating applied to a sustained release drug resin complex utilizing an ion exchange resin with and without a swelling agent was evaluated. The drug release profiles were not significantly impacted by the presence of a swelling agent. Two spectroscopy methods were also used to examine and map the chemical components of the sustained release DRC. Both STXM and SR μ -FTIR were capable of detecting the presence of the components.

INTRODUCTION:

Ion exchange resins such as Sodium Polystyrene Sulfonate have been used in pharmaceutical applications to provide taste masking and sustained-release of a large number of drugs [1,2]. While the ion exchange mechanism is well understood, the effects of the drugs molecular/crystalline state and distribution within the ion exchange resin structure are not well understood. Information about the molecular state of the drug in an ion exchange resin is rare. The role of swelling agents and modifying molecules have been established empirically but the physical basis for their effects are not well understood. The rate of drug loading is affected by the activity of the drug, it's molecular dimensions and the degree to which the resin is swollen during loading. Swelling of the resin aids in the loading process, but may also play a vital role in the performance of the applied coatings which extend the drug release profile over an 8 to 12 hour period. This paper will present drug release results and preliminary spectroscopic examination of an encapsulated drug loaded Sodium Polystyrene Sulfonate ion exchange resin material.

EXPERIMENTAL METHODS:

Materials: Amberlite IRP69 (Rohm and Haas) cation exchange resin, Dextromethorphan HBr USP, Sorbitol, Ethylcellulose and Dibutyl Sebecate were used.

The drug resin complex (DRC) was prepared, loaded and treated as per US Patents 4,221,778 and 4,847,077. The resin was weighed and suspended in water followed by the addition of Dextromethorphan HBr to form the DRC. The mixture was stirred at room temperature (20°C) for 4 hours. The DRC was isolated by filtration and oven dried at 30°C. A portion of the dried DRC was further treated for 20 minutes with a Sorbitol solution (42% w/w) and dried.

An 8% solids coating solution of Ethylcellulose and Dibutyl Sebecate (10%) was applied from a

mixture of Acetone:Methanol in a Wurster Fluid Bed Coating Unit at Coating Place, Inc.

Dissolution tests were performed in simulated gastric fluid, 0.1N HCl for 12 hours. The temperature was 37°C and the paddle speed was 150 rpm.

Samples for Near Edge X-ray Absorption Fine Structure (NEXAFS) Spectroscopy and Synchrotron Radiation micro-FTIR (SR μ -FTIR) were prepared embedding the coated DRC materials in polymer and sectioned using an Ultra-cryo microtome. NEXAFS samples were sectioned 50 to 200 nm thick. SR μ -FTIR was performed on the remaining block sample in reflectance mode.

SR μ -FTIR spectra were collected on BL 1.4.3 of the Advanced Light Source at Lawrence Berkeley National Laboratory over a range of 400 cm^{-1} to 4000 cm^{-1} using a Nicolet Magna 760 FTIR bench and a 10 μm irradiated spot size.

NEXAFS data was collected on the polymer Scanning Transmission X-ray Microscope (STXM) BL 5.3.2 of the Advanced Light Source at Lawrence Berkeley National Laboratory over a range of 280 eV to 340 eV with a spatial resolution of 50 nm.

RESULTS AND DISCUSSION:

The average active drug assay for the untreated and treated DRC samples were 38.6% and 35.1%, respectively. Representative dissolution curves are shown in Figure 1. The presence of the swelling agent did not alter the performance of the applied coating.

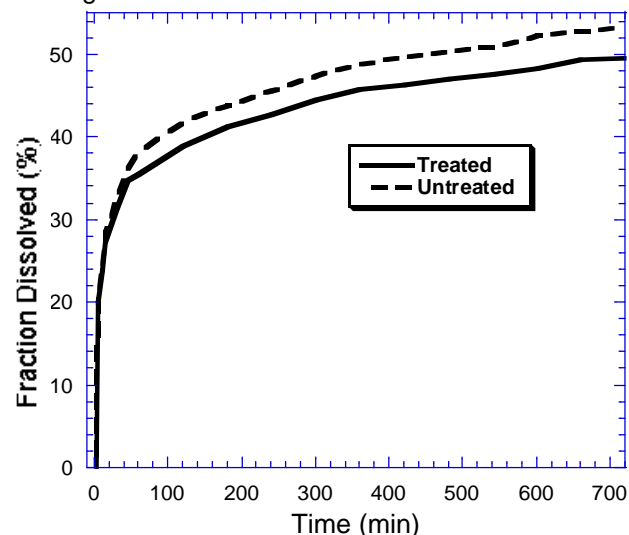


Figure 1. Representative dissolution curves for untreated and treated DRC materials at coated with Ethylcellulose/Dibutyl Sebecate. 15% coat level.

NEXAFS data were collected over the Carbon K-absorption edge on a coated DRC particle treated with a swelling agent. Variations in the carbon chemistry of the particle, coating material and polymer mounting material can be seen in Figure 2. The NEXAFS spectra contain variations in intensity and peak position. The Ethylcellulose coating material has been distinguished from the Sodium Polystyrene Sulfonate and methacrylate mounting material. Within the DRC there are subtle attenuation variations in the NEXAFS images. These variations are from several sources. First is natural variations in the structural density of the ion exchange resin. The other source is variations in the concentration of Dextromethorphan HBr present.

SR μ -FTIR spectra were collected as line and area maps with point-to-point spacing of 10 μ m. The spectral maps started in the methacrylate mounting material and traversed through the coating and into the DRC. Reflectance peaks associated with Sorbitol were only seen in the near surface region.

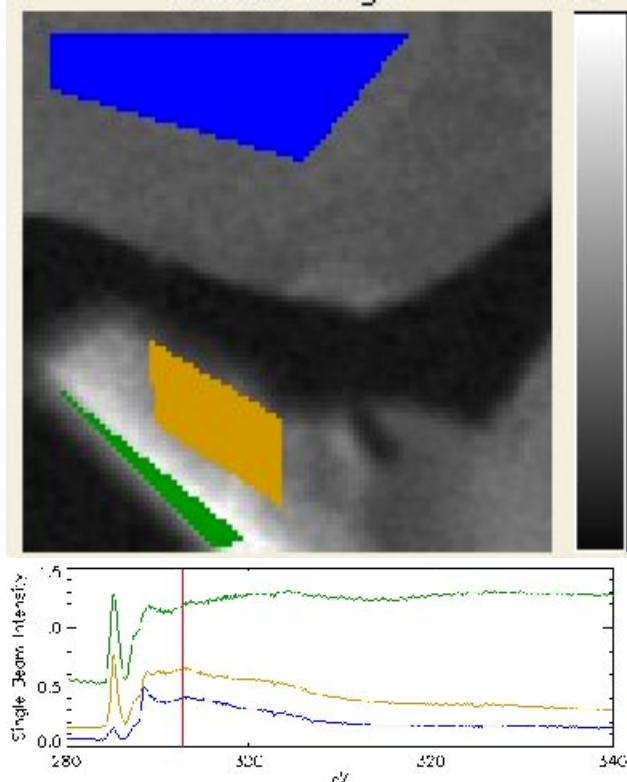


Figure 2. STXM image of an area 10 μ m x 10 μ m. The variations in carbon chemistry for the three regions are represented in the NEXAFS spectra. (Regions top, middle and bottom correspond to the bottom, middle and top spectra, respectively.)

CONCLUSIONS:

When an Ethylcellulose coating is applied under appropriate conditions, the drug release profile is not significantly enhanced or degraded by the presence of a swelling agent. SR μ -FTIR and STXM indicate the presence of swelling agent at the surface of ion exchange resin particles. Samples treated with a

swelling agent for a period of 20 minutes did not indicate the presence of swelling agent deep in the ion exchange resin.

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