Modulation of Ciprofloxacin Release from Sol-Gel Derived Silica Matrices

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Statement of Purpose: The research goal was to determine whether the release of a model antibiotic, Ciprofloxacin, from a biocompatible, resorbable, sol-gel derived SiO_2 matrix could be modulated through variation in the gel textural properties and degree of loading. Better control over antibiotic release may allow for use in localized delivery applications.

Methods: Sol-gel derived silica glasses were prepared by either acid (HCl) or base (NH_3OH) catalyzed hydrolysis of tetraethylorthosilicate (TEOS, Acros Organics) and the subsequent polycondensation of $Si(OH)_4$. Ciprofloxacin (Sigma-Aldrich) was added to sols at a concentration of 0.1 or 0.5 weight percent relative to the final SiO_2 content. Gel aging took place for 4 d at 22°C. Textural properties (pore diameter, size distribution, specific volume and BET surface area) were characterized using N_2 physisorption (Micromeritics ASAP 2020). FTIR spectroscopy (Matson Genesis II) was used to further examine the glass structure. Thermogravimetric and differential thermal analysis were performed using a TA Instruments SDT Q600. Triplicate samples of antibiotic-loaded or control sol-gel particulate (1.00 g, 38-90 µm) were each immersed in 20 ml 0.04 M Tris buffer (37ºC) and rotated at 80 rpm. At prescribed time points 500 µL solution was removed for analysis and replaced with 500 µL fresh buffer. Ciprofloxacin release was measured directly at 270 nm using a BioTek Synergy HT spectrophotometer whereas Si release was measured at 810 nm using a modified molybdenum blue technique.

Results/Discussion: Nitrogen sorption analysis revealed pronounced differences between the textures of Ciprofloxacin loaded HCl and NH_3OH catalyzed gels. Acid catalyzed gels were predominantly microporous (<20Å pore radius), whereas NH_3OH catalyzed glasses (Fig. 1, 0.1 wt. %) were primarily mesoporous (215-260 Å). The BET surface area values for 0.1 and 0.5 wt % Ciprofloxacin acid catalyzed gels were 0.5 and 139 m^2/g, respectively.

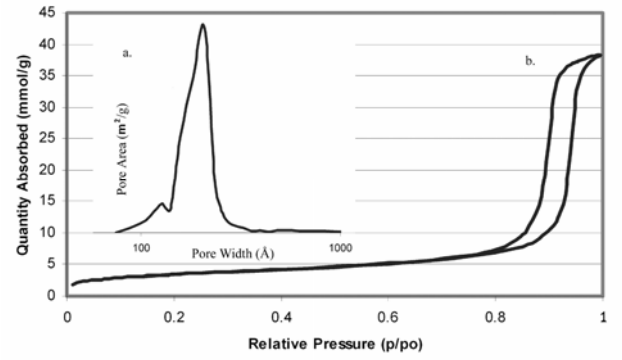

Figure 1. N_2 sorption analysis: (a) pore size distribution and (b) isotherm (0.1% Ciprofloxacin, base-catalyzed).

Fig. 2 demonstrates that wide ranging, clinically relevant [1,2], Ciprofloxacin release profiles could be achieved, especially within the first hours when prevention of bacterial colonization can be critical. Texture strongly influenced Ciprofloxacin release from HCl catalyzed gels. Release from both 0.5% Ciprofloxacin acid and base catalyzed gels was diffusion controlled between 1-48 hr.

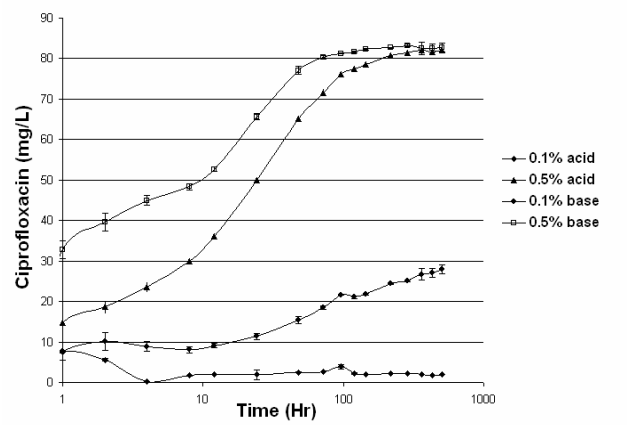

Figure 2. Ciprofloxacin release from acid (HCl) and base (NH_3OH) catalyzed silica gels.

Structural changes induced by the addition of Ciprofloxacin to the sol-gel were evidenced by shifting of the Si-O-Si stretching vibration to a lower wavenumber. The resorbable nature of the matrix is shown in Fig 3; solution Si concentrations for each treatment were similar after 7 d due to solution saturation.

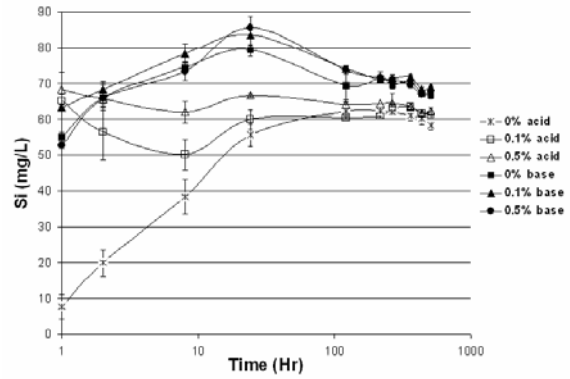

Figure 3. Si release from silica gel matrices.

Conclusion: Pronounced variation in the release profile of Ciprofloxacin from resorbable sol-gel derived silica matrices can be attained through variation in the gel textural properties and degree of loading.

References: [1] Tunney MM. Antimicrob Agents Chemother. 1998; 42:3002-5. [2] Turkmani A. Ann Clin Microbiol Antimicrob. 2006;5:24.