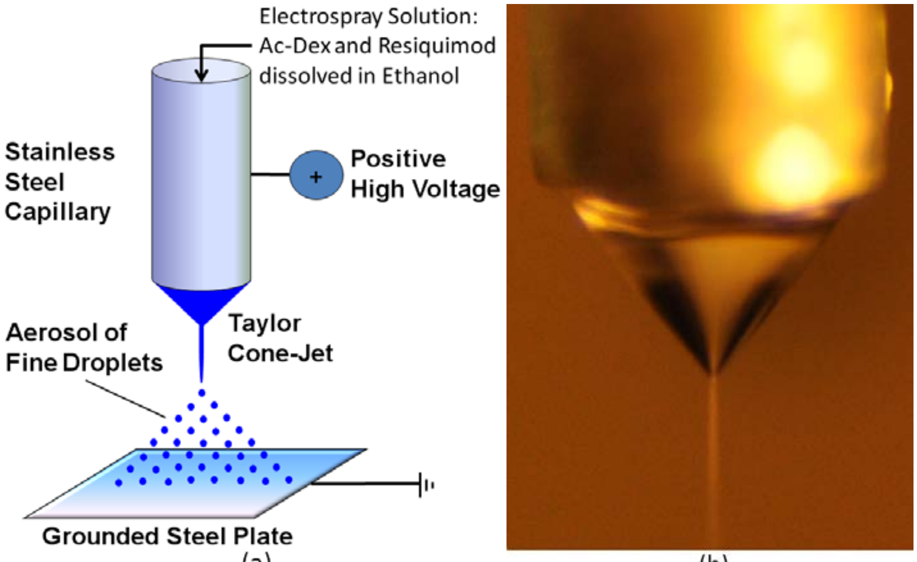
SUPPLEMENTARY MATERIAL



(a) (b)

Figure S.1. (a) In the experimental set up for single capillary electrospray fabrication of microparticles, a high positive voltage was applied to a nozzle tip positioned 7 cm above a 58 cm^2 grounded stainless steel collection plate. (b) A typical Taylor Cone Jet observed during electrospray fabrication of Ac-DEX particles from a solution of 50 mg/mL Ac-DEX in ethanol.

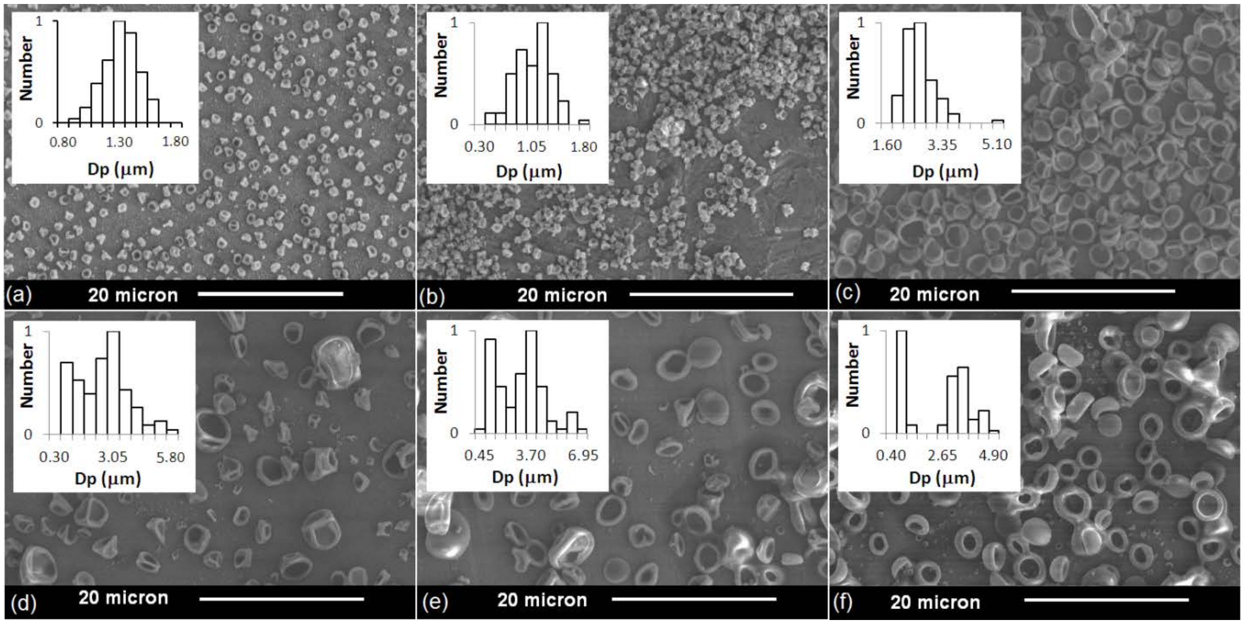


Figure S.2. SEM images from Figure 1 along with number weighted particle size distributions measured using ImageJ software. The mean particle diameter by number for ethanol (b) is in good agreement with that which is measured from dynamic light scattering shown in Figure 2.

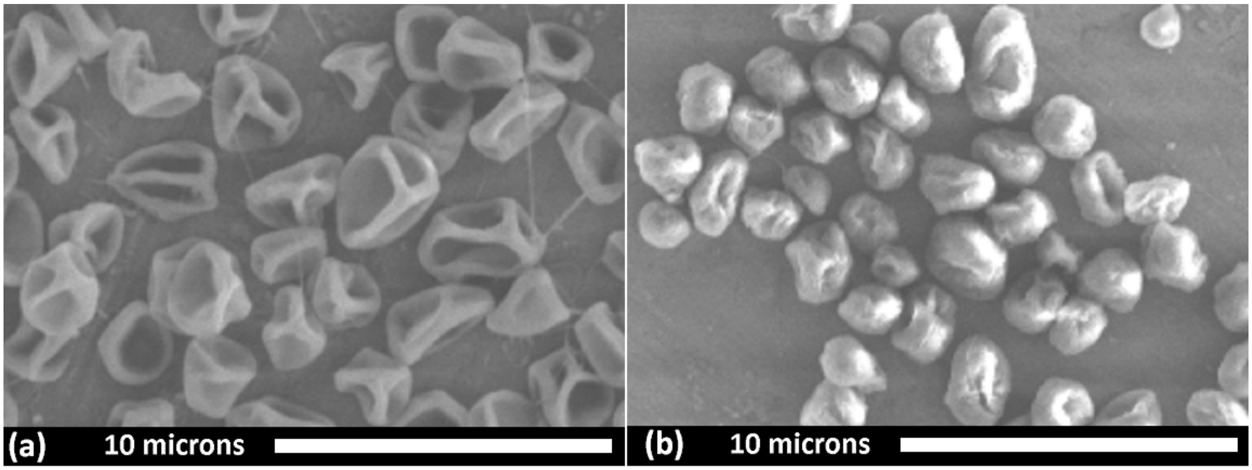


Figure S.3. SEM images of electrosprayed Ac-DEX/Tween blended particles (10 % Tween by mass). Ac-DEX particles blended with Tween 20 (a) and Tween 80 (b).

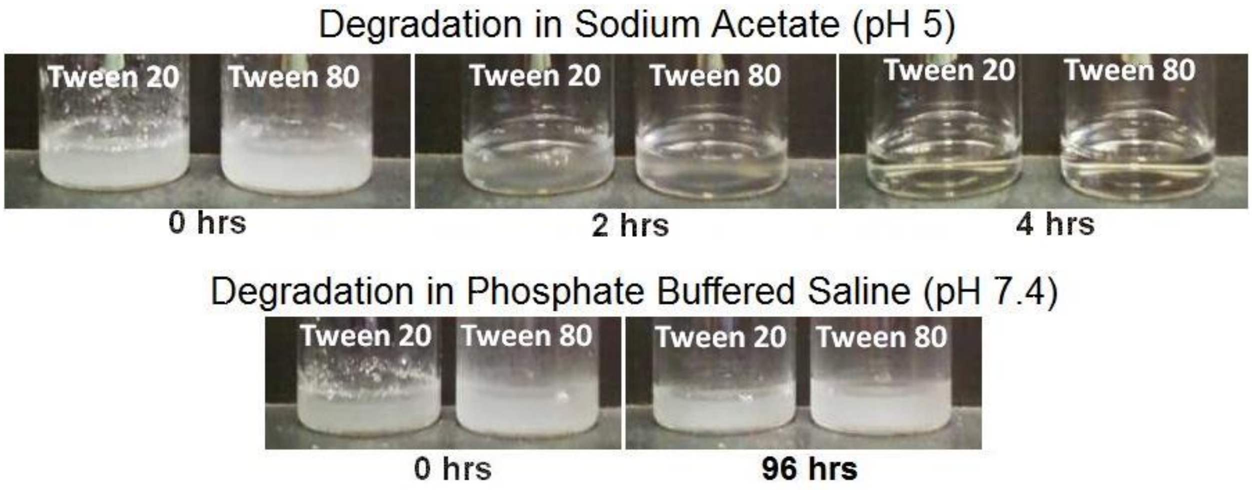


Figure S.4. Time lapsed photographs of the electrosprayed Ac-DEX/Tween composite particles. The top row of images show the particles dispersed in sodium acetate buffer (pH 5) at 0, 2 and 4 hours after being dispersed. The bottom two images show the particles dispersed in phosphate buffered saline (pH 7.4) at 0 and 96 hours after dispersion. In each image, the vial on the left contains particles made with Tween 20, and the vial on the right, Tween 80.

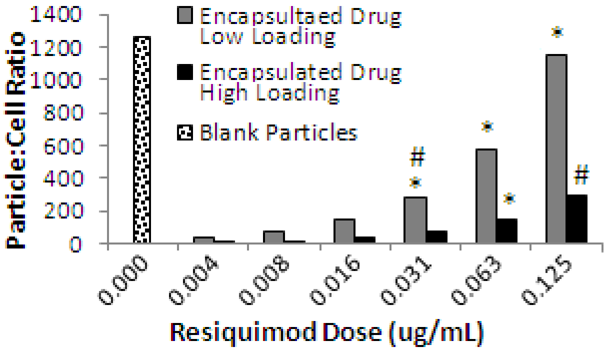


Figure S.5. The estimated particle to cell ratio increases with the resiquimod concentration. An * indicates a significant decrease in cell viability compared to free drug at the same dose. A # indicates the drug levels for which the nitrite production was maximized.

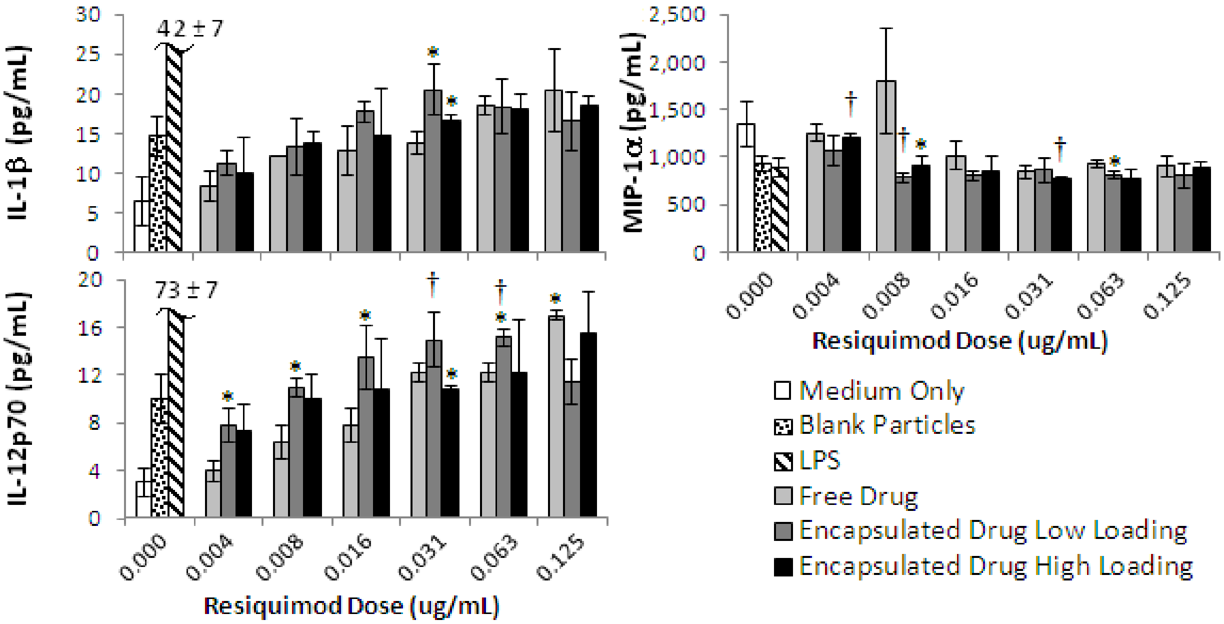


Figure S.6. Concentration of three inflammatory cytokines measured along with the ones reported in Figure 6. These concentrations are either too low to be considered practically significant (IL-1 β and IL-12p70), or lack statistical significance compared to free drug or blank particles (MIP-1α). MIP-1α concentrations are below the background concentration in cells grown in pure medium. An * indicates significant difference with respect to free drug at the same dose ($p < 0.05$). A † indicates a significant difference relative to the blank particle control ($p < 0.05$).

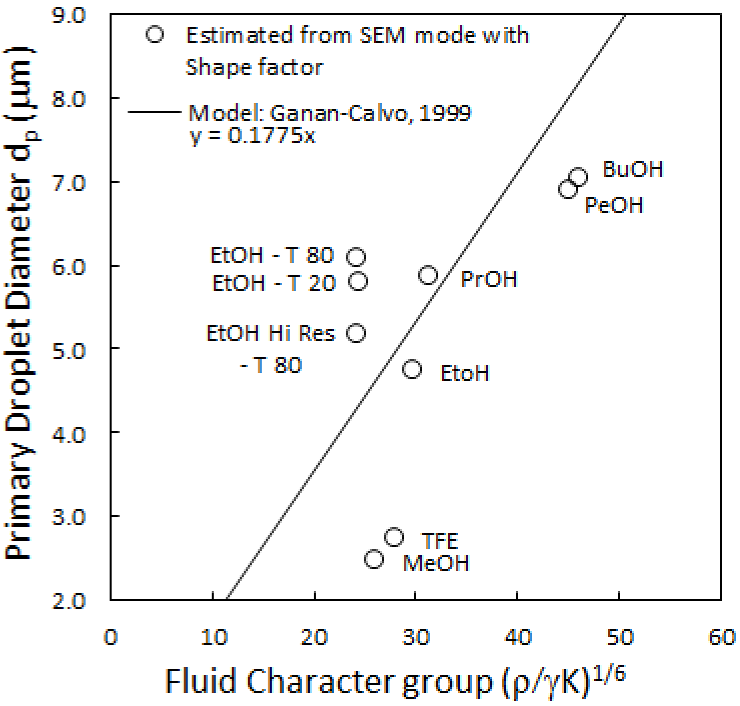


Figure S.7. The primary droplet sizes (open circles) determined experimentally from SEM image analysis and Eq.2 are within 50% of the values predicted by the scaling law of Ganan-Calvo et al. (solid line) that predicts the primary droplet size produced from an electrospray in the cone-jet mode should follow [37].

$$d_p = \alpha \left(\frac{Q^3 \varepsilon_0 \rho}{\pi^4 \gamma K}\right)^{1/6} \qquad \text{Eq. S.1}$$

Here, α is a dimensionless constant with a value of 2.9 and ε_0 is the permittivity of a vacuum.[61] Q is the flow rate of the electrospray solution. ρ, γ and K are the flow rate, density, surface tension and conductivity of the electrospray solution respectively. Literature values for the pure solvent were used for these variables.[24, 62-64] If the flow rate, Q, is also held constant, then a plot of primary droplet size versus $(\rho/\gamma K)^{1/6}$ should be a straight line with a slope of $(Q^3\varepsilon_0/\pi^4)^{1/6}$. This is the solid line plotted in Fig S.6.

The experimentally estimated primary droplet size was calculated using equation 2.

$$D_d = D_p \left(\chi \frac{\rho_p}{C_p} \right)^{1/2} \qquad \text{Eq. S.2}$$

The shape factor χ accounts for the degree to which the particle morphology is collapsed. When particles are spherical, the shape factor equals 1. When particles are collapsed and assume the shape of a disc, the shape factor is the fraction of polymer volume that in a disc with radius r and height h compared to that in a sphere with radius r_1. The values of r and h are measured using ImageJ [28].

Calculation of the Peclet Number

$$Pe = \frac{Solvent\,Evaporation}{Polymer\,Diffusion} \frac{D_{solvent,air} \dfrac{\rho_{gas}}{\rho_{solvent}} \ln\left(1 + \dfrac{m_{vap,0} - m_{vap,\infty}}{1 - m_{vap,0}}\right)}{D_{polymer,solvent}} \qquad \text{Eq. S.3}$$

The gas phase diffusion coefficients for solvent vapor in air at 20°C ($D_{solvent,air}$) were taken from the literature.[65] The diffusion coefficient of Ac-DEX in the solvent ($D_{polymer,solvent}$) was calculated using the modified Scheilbel and Wilke-Chang equation.[29] The density of the liquid solvent ($\rho_{solvent}$) is also available in literature [62] and the density of the surrounding gas (ρ_{gas}) was calculated using the ideal gas law. The value of the vapor phase solvent mass fraction at the droplet surface ($m_{vap,0}$) was calculated using the ideal gas law and the saturation vapor pressure assuming the droplet is at room temperature. The saturation vapor pressure was calculated using the Antoine Equation and parameters from Yaw's Handbook.[66] Finally, perfect sink conditions were assumed so that the vapor phase solvent mass fraction in the bulk air ($m_{vap,\infty}$) was set to zero.

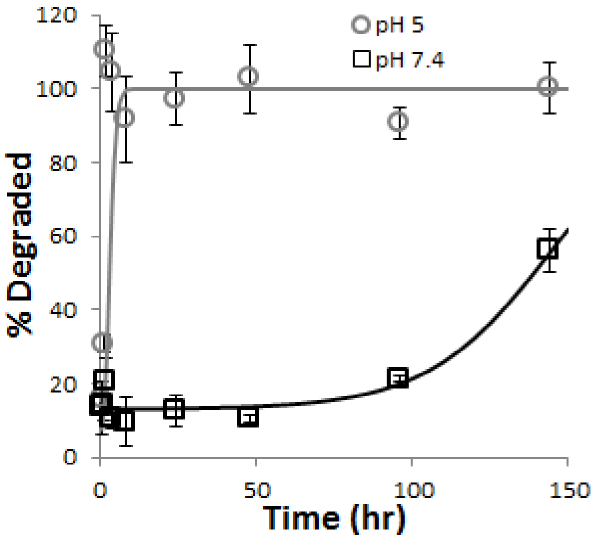


Figure S.8. The particle degradation profile measured for blank Ac-DEX/Tween 80 microparticles from the resiquimod release profiles. Briefly, the wells containing supernatants from blank Ac-DEX/Tween 80 particle suspensions used as a background for the resiquimod release profile experiment were analyzed for the presence of degraded Dextran using a Bichinchoninic Acid (BCA) assay. Data points show the mean of triplicates and the error bars show the standard deviation. As expected, the polymer degradation rate is much slower at pH 7.4 than at pH 5.