Electronic Supplementary Information

Electrically Controlled Release of Insulin using Polypyrrole Nanoparticles

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A) TEM images of PPy NPs

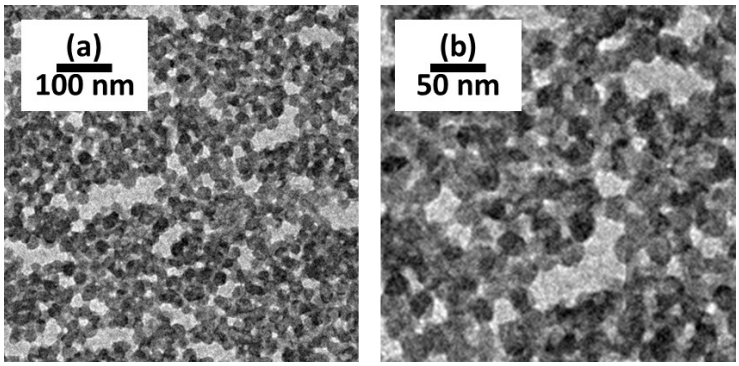

Figure S1. Typical TEM images of PPy NPs at two different magnifications. These images were obtained using a FEI Tecnai G2 F20 X-TWIN Transmission Electron Microscope.

B) Model for insulin (INS) binding onto surface of polypyrrole nanoparticles (PPy NPs)

The first step toward understanding the binding of INS to PPy NPs is to identify whether the binding is reversible or irreversible. If irreversible binding is to be assumed, when the number of INS molecules is lower than the number of available "binding sites", the number, and hence, the concentration of free INS should be zero. However, it was observed that regardless of how low was the concentration of initially added INS, some INS always remained free. This observation suggested that the binding may be reversible, the INS being partitioned between the aqueous phase and the solid nanoparticulate phase.

To verify reversible binding, we developed a binding model, making the following assumptions:

1. One INS molecule binds to one "binding site" on the surface of a PPy NP.
2. On an average, the number of binding sites per PPy NP is constant.
3. After mixing INS solution with PPy NPs, equilibrium is attained, with a binding equilibrium constant *K*.
4. *K* is independent of the number of INS molecules attached to the PPy NPs.

Let the subscripts have the following meaning: i = initial; b = bound; f= free; and eq = equilibrium. We also introduce the notation where [INS], [BS], and [INS-BS] are the molar concentrations of insulin, the binding sites of PPy NPs, and the bound insulin. This model assumes the reversible reaction INS + BS ↔ INS-BS. Then it is easy to develop the following expression for *K*

$$K = \frac{[\text{INS-BS}]_{eq}}{[\text{INS}]_{eq}[\text{BS}]_{eq}} = \frac{[\text{INS}]_b}{[\text{INS}]_{eq}\{[\text{BS}]_i - [\text{INS}]_b\}} = \frac{[\text{INS}]_b}{[\text{INS}]_f\{c[\text{PPy}]_i - [\text{INS}]_b\}} \quad (1)$$

where *c* is a proportionality constant. We define

$$\theta = \frac{[\text{INS}]_b}{c[\text{PPy}]_i} \quad (2)$$

which allows us to rewrite eq. (1) as

$$\frac{1}{\theta} = 1 + \frac{1}{K[\text{INS}]_f} \quad (3)$$

It should be noted that eq. (3) describes a Langmuir-type adsorption model, where θ is the fraction of binding sites occupied by INS, and this fraction increases as the concentration of INS initially added is increased. We can recast eq. (3) in the form

$$\frac{c[PPy]_i}{[INS]_b} = 1 + \frac{1}{K[INS]_f} \quad (4)$$

It is convenient to switch to the weight of a compound per unit volume denoted by *W(x),* and *MW(x)* is the molecular weight of *x*. Then eq. (4) becomes

$$\frac{\frac{cW(PPy)_i}{MW(PPy)}}{\frac{W(INS)_b}{MW(INS)}} = 1 + \frac{1}{\frac{KW(INS)_f}{MW(INS)}} \quad (5)$$

or equivalently

$$\frac{cMW(INS)W(PPy)_i}{MW(PPy)W(INS)_b} = 1 + \frac{MW(INS)}{KW(INS)_f} \tag{6}$$

Eq. (6) may be rewritten as

$$\frac{W(PPy)_i}{W(INS)_b} = \frac{MW(PPy)}{cMW(INS)} + \frac{MW(PPy)}{cKW(INS)_f} \tag{7}$$

By defining $\theta' = W(INS)_b/W(PPy)_i$, intercept = $MW(PPy)/cMW(INS)$, and slope = $MW(PPy)/cK$, we obtain the equation

$$1/\theta' = \text{intercept} + \text{slope}/W(INS)_f \tag{8}$$

By plotting $1/\theta'$ versus $1/W(INS)_f$, a straight line should be obtained, with a positive slope and positive intercept. Experimental data fit this linear model well, with a R^2 value of 0.993. The equilibrium constant K may be calculated from the slope. From the intercept, the maximum drug loading may be calculated as follows:

The drug loading DL in weight percent is given by

$$DL = \frac{W(INS)_b}{W(INS)_b + W(PPy)_i} \bullet 100 = \frac{1}{1 + \frac{W(PPy)_i}{W(INS)_b}} \bullet 100 \tag{9}$$

Maximum drug loading percentage is obtained when all the binding sites are occupied, i.e., when θ=1. Thus, we find

$$DL_{\max} = \frac{1}{1 + \text{intercept}} \bullet 100 \tag{10}$$

From experimental data, the maximum drug loading percentage is calculated to be ~51 wt %.

C) INS release for *in vivo* tests

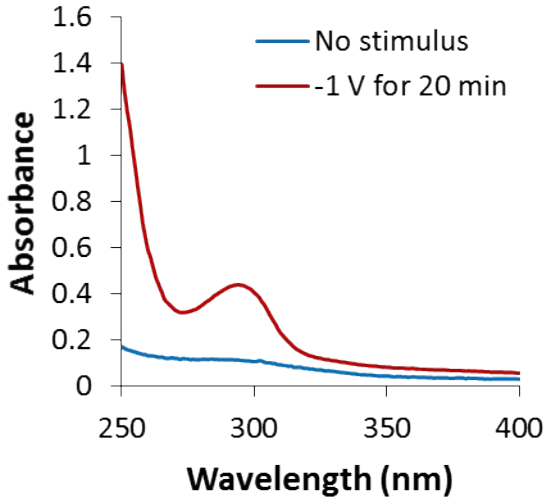

Figure S2. Absorbance spectra of INS released from PPy NPs with and without electrical stimulus. As can be seen, a negligible amount of INS is released without stimulus. The absorbance of INS released on application of stimulus here corresponds to an absolute amount of ~500 µg.