Polymer Tissue Partition Coefficient in Implant Leaching and Biotransport

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Hazardous materials contained within an implanted polymeric medical device can pose a risk when they leach into the body at a high enough rate. Mathematical models and computer simulations that utilize semi-empirical methods that consider structural properties have started to provide new insight into migration within these systems. This presentation highlights recent work to better understand biotransport across the polymer-tissue interface. Migration of chemicals across the boundary of an implant is influenced by the polymer-tissue partition coefficient, $K_{p:t}$. It describes how a chemical of interest will distribute between the two materials after achieving equilibrium. The proportion that will dissolve in one material or another is based on the relative solubility of the chemical within that material. The value is important in biotransport models because it influences the concentration at the surface and as a result, impacts the concentration gradient driving diffusion. Over the past two decades several models have been developed to describe the partition coefficients of chemicals between two different types of biological tissue. In addition, polymer-water partition coefficients for thousands of polymer / chemical combinations have been aggregated. Utilizing these works, the polymer-tissue partition coefficient was calculated for a multitude of different polymers and leachable chemicals. $K_{p:t}$ was calculated using the equation $K_{p:t} = S_p / S_t$, where S_p is the solubility of a chemical in the polymer and S_t is the solubility of a chemical in the tissue. The solubility of a chemical in the tissue can, in turn, be estimated from the solubility of a chemical in water, the octanol-water partition coefficient, $K_{o:w}$, and the volume fractions of neutral lipids, phospholipids, and water within the tissue, $S_t = f(S_w, K_{o:w}, V_{n:t}, V_{ph:t}, V_{w:t})$. Using this approach, S_t was found for 58 chemicals in 9 different tissue types using published literature and online sources. The solubility of thousands of chemical / polymer combinations was obtained from the polymer water partition coefficients and water solubilities. Upon examination, two regimes emerged in the $K_{p:t}$ values. Chemicals with a lower octanol-water partition coefficient ($K_{o:w} < 1.5$) had a polymer-tissue partition coefficient that was proportional to the octanol-water partition coefficient ($K_{p:t} \approx 0.0269 K_{o:w}$). However, chemicals with a higher octanol-water partition coefficient ($K_{o:w} > 1.5$) had a polymer-tissue partition coefficient that was generally constant ($K_{p:t} \approx 2.69$). These findings imply that the polymer-tissue partition coefficient may be bounded, which has implications on the rate of biotransport. By bounding the partition coefficient, the inhibiting effect of the partition coefficient on the concentration gradient within the polymer is also bounded. Yet, even with this upper bound the effect of partitioning could reduce the predicted diffusion rates by 4 to 28 times by including it in the model. More work is needed to determine if the inclusion of $K_{p:t}$ in mathematical models used to predict the quantity of leachable chemicals released from an implanted device will improve the model's predictive capability.