OMICS International
conferenceseries.com

Pharm Anal Acta 2016, 7:1 (Suppl)
http://dx.doi.org/10.4172/2153-2435.C1.028

8th International Conference and Exhibition on

Pharmaceutics & Novel Drug Delivery Systems

March 07-09, 2016 Madrid, Spain

A hierarchical strategy for mathematical modeling of drug dissolution and the importance of shear-rate in determining *in-vivo* relevance of *in-vitro* dissolution

James G Brasseur[1], **Yanxing Wang**[2], **Deanna Mudie**[3] and **Gregory E Amidon**[3]
[1]University of Colorado, USA
[2]Georgia Institute of Technology, USA
[3]University of Michigan, USA

We present an advanced strategy for practical mathematical predictions of dissolution from clouds of small drug particles with initial specified dose and particle size distribution within an impermeable container. The strategy is hierarchical in nature with an accurate first-principles model for diffusion-dominated dissolution at its core, systematically extensible to include alterations to dissolution from local hydrodynamic influences as well as form the confined nature of dissolution local to individual particles. With the model, we describe the sensitivities of the predictions to details of the initial size distribution. With appropriate non-dimensionalization of model predictions, we show that dissolution can be categorized as: (1) well approximated by sink conditions, (2) dominantly influenced by confinement or (3) strongly impacted by a "saturation singularity" when dose concentration and solubility total are similar. With a mass transport analysis using computational fluid dynamics we have shown that local fluid shear rate is a dominant hydrodynamic effect that enhances dissolution rate over pure diffusion and that distinguishes *in-vivo* from *in-vitro* dissolution, particularly with respect to USP 2 *in-vitro* dissolution tests. We incorporate shear "correlations" into the hierarchical model structure and compare predictions with an experimental *in-vitro* study using a Couette cell in which shear rate could be precisely controlled. The *in-vitro* data were collected at shear rates consistent with *in-vivo* dissolution and with standard applications of the USP 2 apparatus. Model predictions and experimental data compare well and show strong hydrodynamic enhancement from shear that distinguish *in-vivo* from *in-vitro* dissolution.

James.Brasseur@Colorado.EDU

Surface modified ferritin nanoparticles for imaging and drug delivery

Jin Xie
The University of Georgia, USA

Ferritins are a family of iron storage proteins with ubiquitous distribution among almost all life forms. Ferritins feature a cage-like structure, with an outer diameter of approximately 12 nm and an inner cavity of 7–8 nm. Natural ferritins are always filled with a ferric oxohydroxy core, while artificially made ferritins have an empty cavity at the center. Ferritins are decomposed into 24 subunits when the pH is decreased to 2~3 and when the pH is tuned back to neutral, the subunits will reconstitute into a nanocage in a nearly intact fashion. Such pH-mediated disassembly-and-reassembly provides a facile means to load molecules into ferritins. For instance, we recently reported that chemotherapeutics like doxorubicin can be loaded into ferritins with high efficiency. Moreover, we found that ZnF16Pc, a potent photosensitizer, can be loaded into ferritins by up to 60wt%. Meanwhile, the surface of ferritins can be modified, through either chemical conjugation or genetic engineering, to present tumor targeting ligands. These features of ferritins, along with their intrinsic biocompatibility and biodegradability, suggest great potential of the platform as a novel delivery system. More recently, we found that $ZnF_{16}Pc$-loaded and RGD4C presenting ferritins can home to tumor endothelium; with photo-irradiation at relatively low fluences, the resulting PDT treatment leads permeabilized tumor vasculatures. As a result, macromolecules or nanoparticles administered afterwards are able to extravasate and accumulate more efficiently at the tumor sites. This methodology can artificially enhance the EPR effect of tumors so as to improve nanoparticle delivery to tumors.

Notes:

jinxie@uga.edu